THE LANCET

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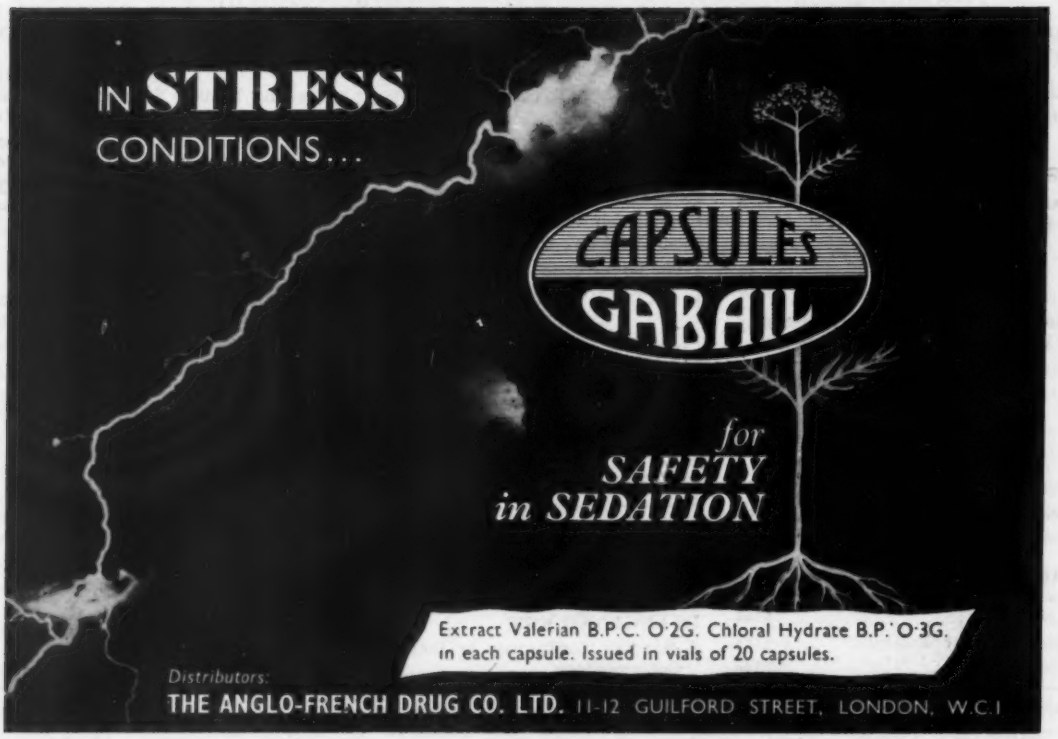

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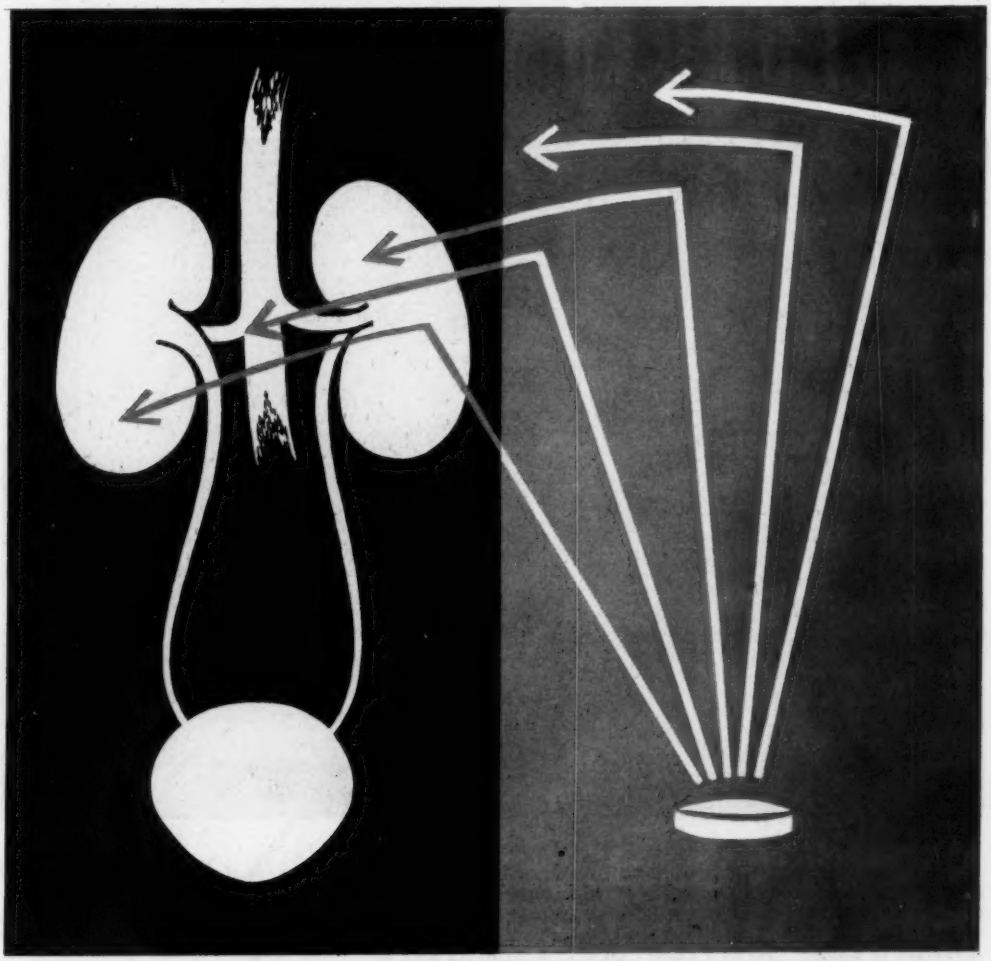

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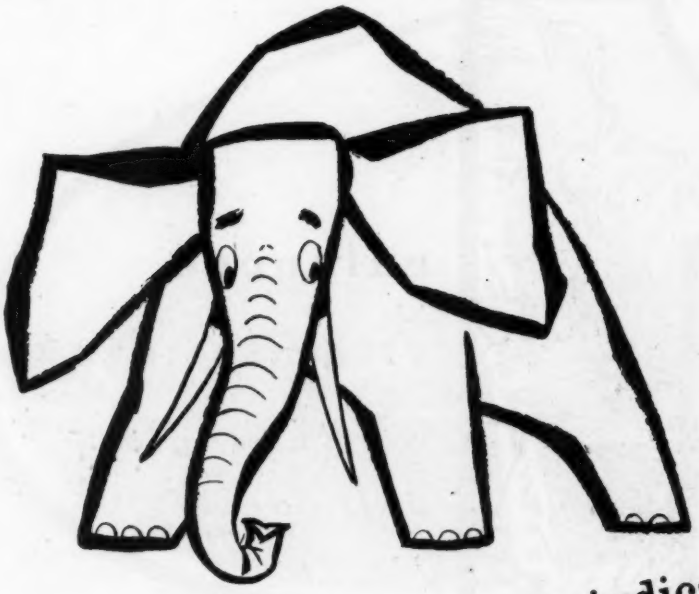

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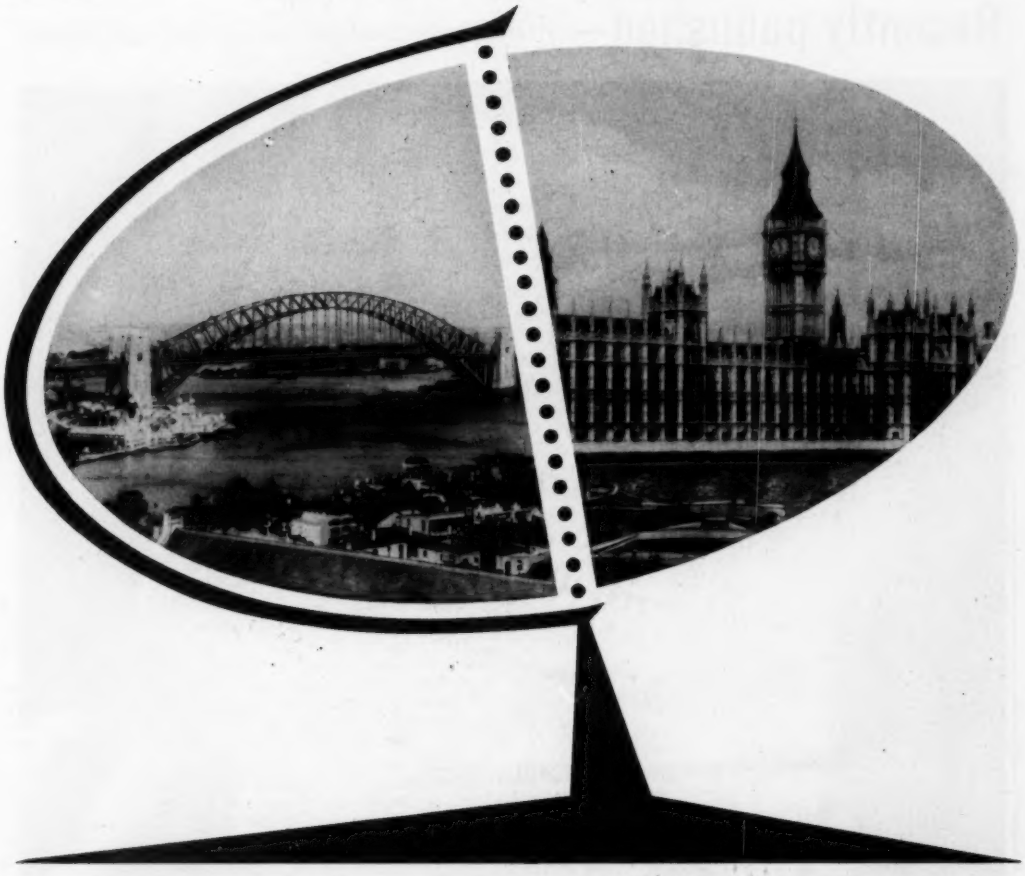

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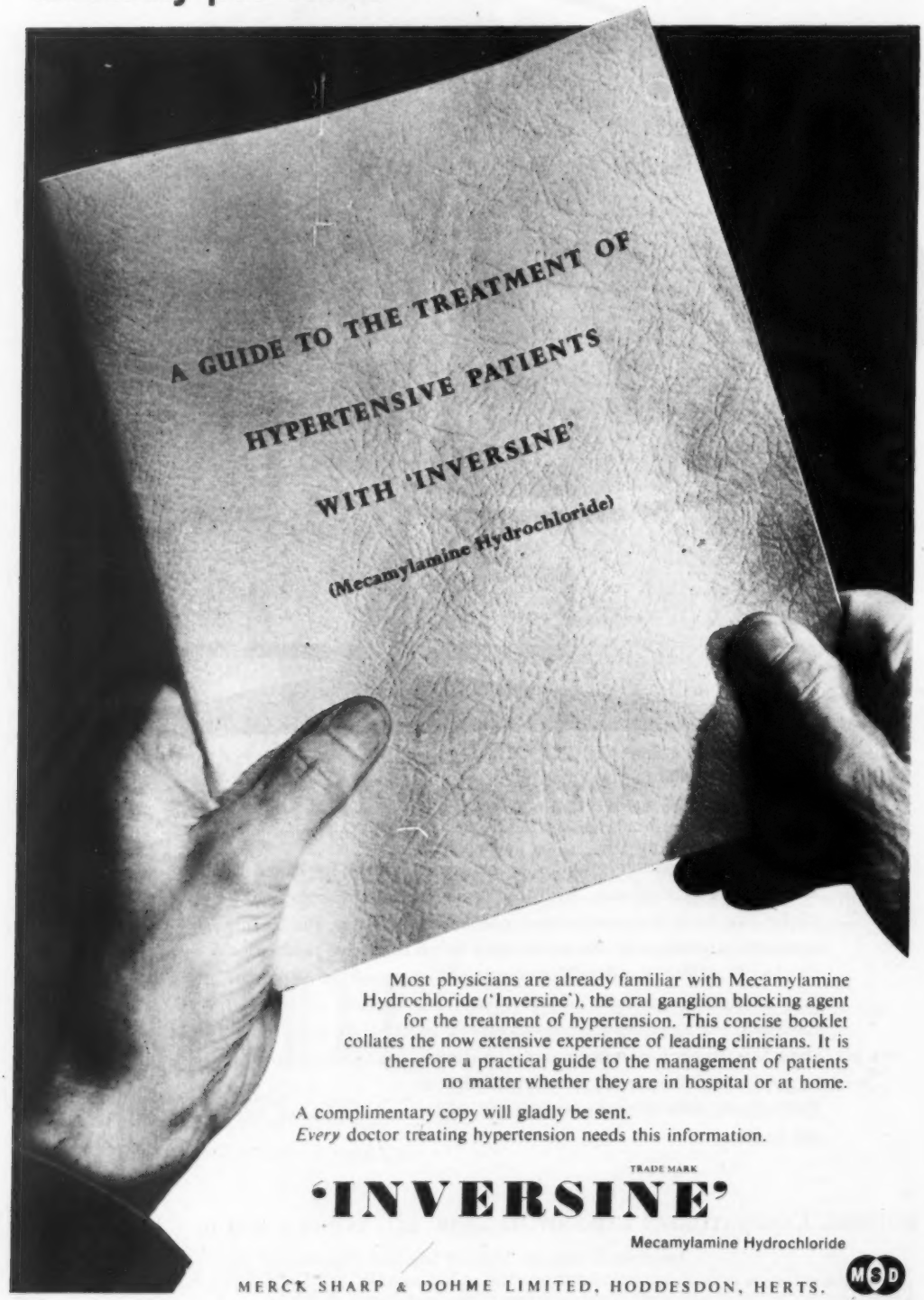

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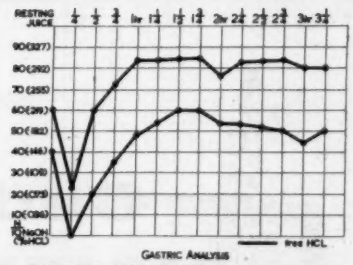
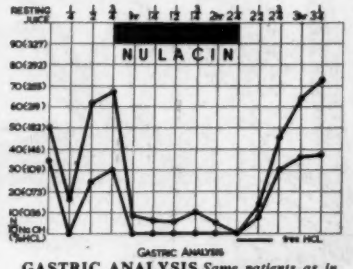
NULACIN tablets are not advertised to the public and have no B.P. equivalent. They may be prescribed on E.C.10. The dispensing unit of 25 tablets is free of purchase tax. (Basic price to N.H.S. . . . 2/-). Also available in tubes of 12.

NULACIN tablets are prepared from whole milk combined with dextrins and maltose, and incorporate magnesium trisilicate 3.5 grs.; magnesium oxide 2.0 grs.; calcium carbonate 2.0 grs.; magnesium carbonate 0.5 grs.; Ol. Menth. Pip. q.s.



GASTRIC ANALYSIS *Superimposed gruel fractional test-meal curves of five cases of duodenal ulcer.*

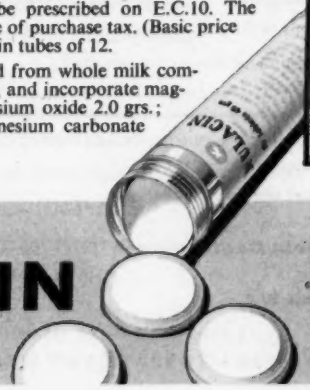


GASTRIC ANALYSIS *Same patients as in Fig. 1, two days later, showing the striking neutralizing effect of sucking Nulacin tablets (3 an hour). Note the return of acidity when Nulacin is discontinued.*

BIBLIOGRAPHY

Practitioner, 1957, **178:** 43
Practitioner, 1956, **176:** 103
Amer. J. Gastro. 1956, **26:** 665
Brit. Med. J. 1954, **1:** 46

Further references to the literature and full information on Nulacin available on request.



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have I been disappointed in this expectation... The more I saw of the great powers of this plant, the more it seemed neceſſary to bring the doſes of it to the greateſt poſſible accuracy. I [illegible] this degree of [illegible] was not

— William Withering, M.D., 1785

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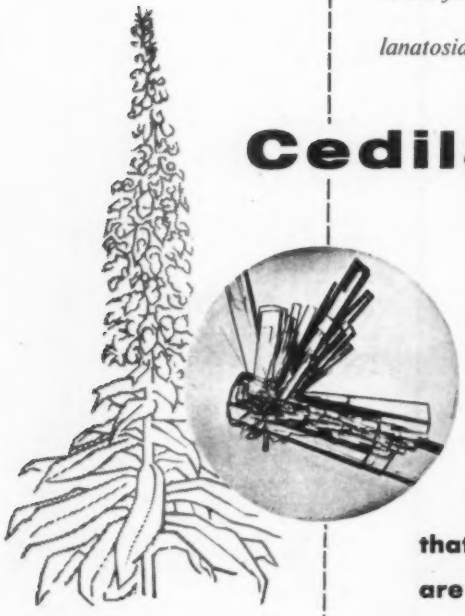

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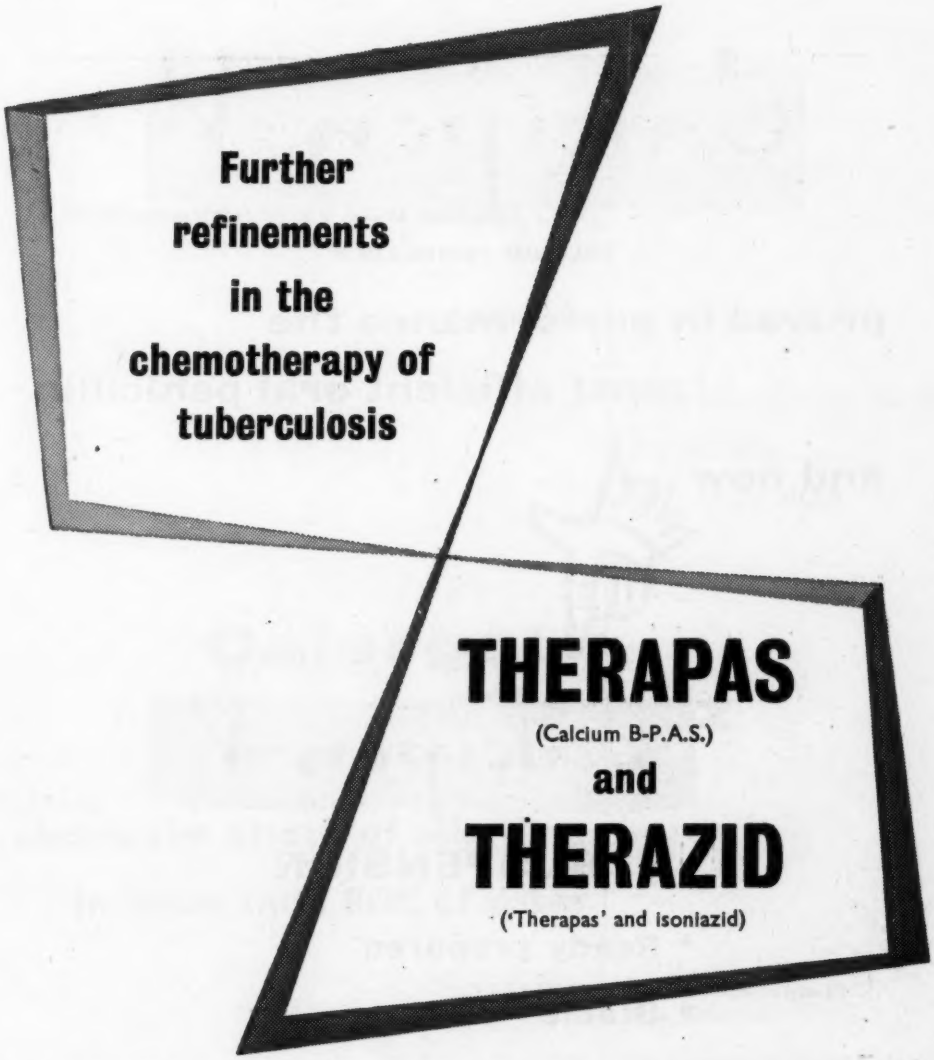

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Each 'Theodrox' tablet contains 3 grains aminophylline and 4 grains dried aluminium hydroxide gel. 'Theodrox' is also available combined with ⅛ grain phenobarbitone where a degree of sedation is also required.

REFERENCES

1. *Brit. Med. J.* (1957) *2*: 67
2. *Ibid.*, page 274

DOSAGE . . .

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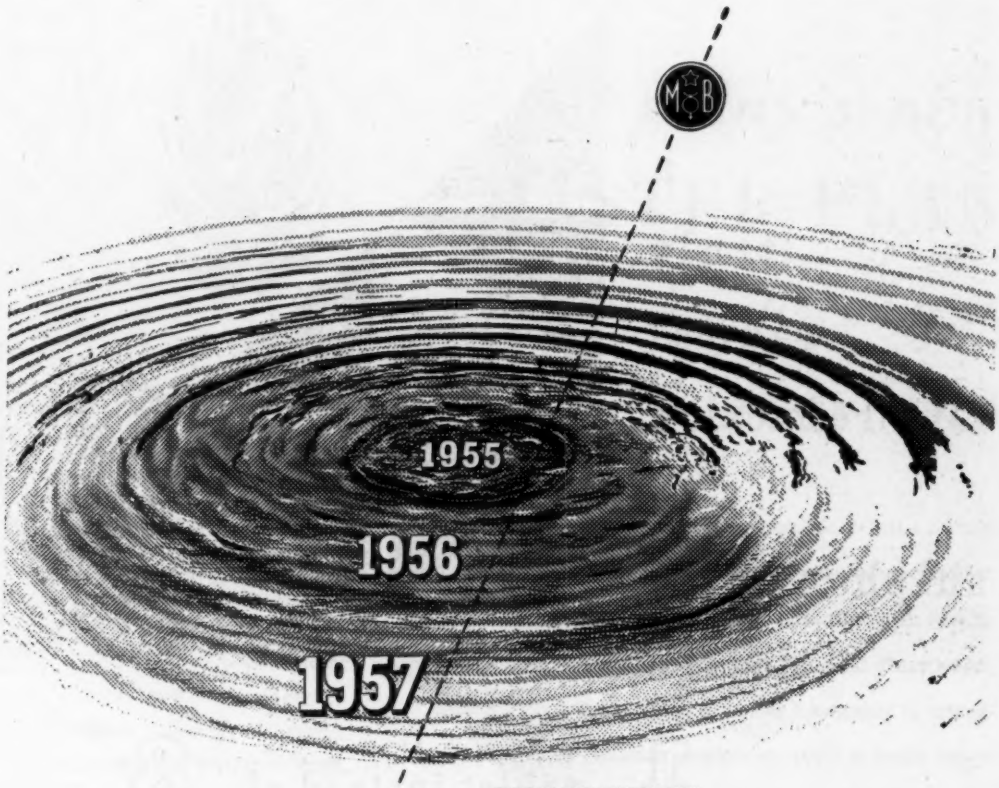

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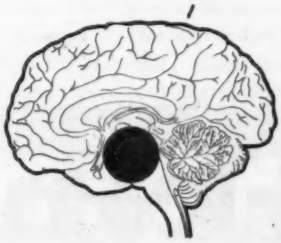

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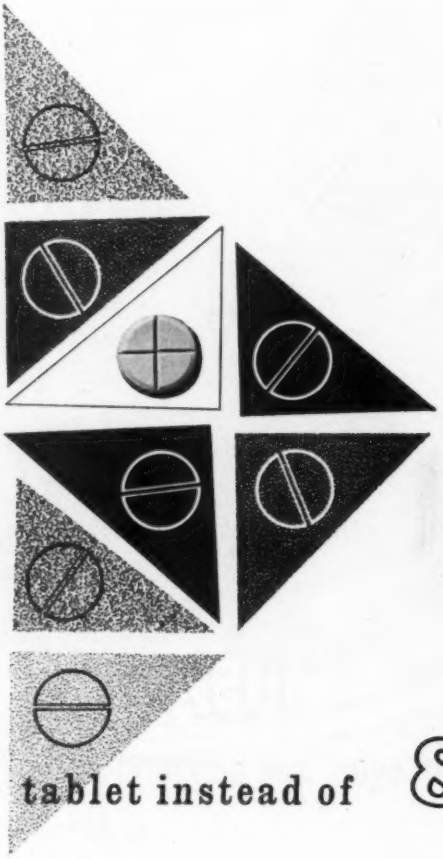

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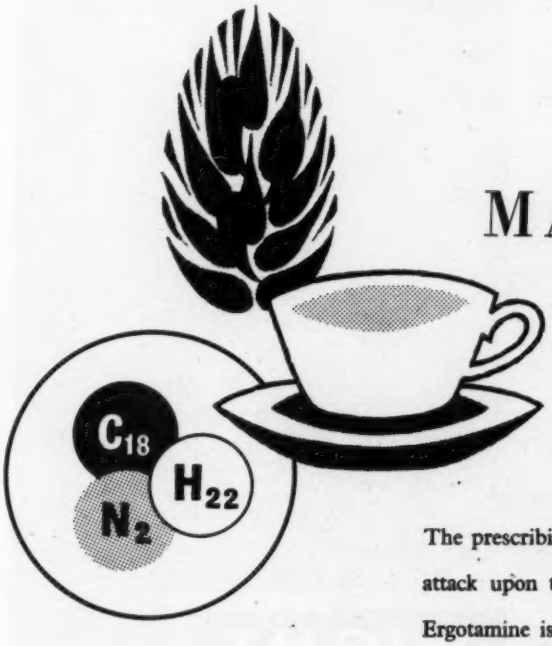

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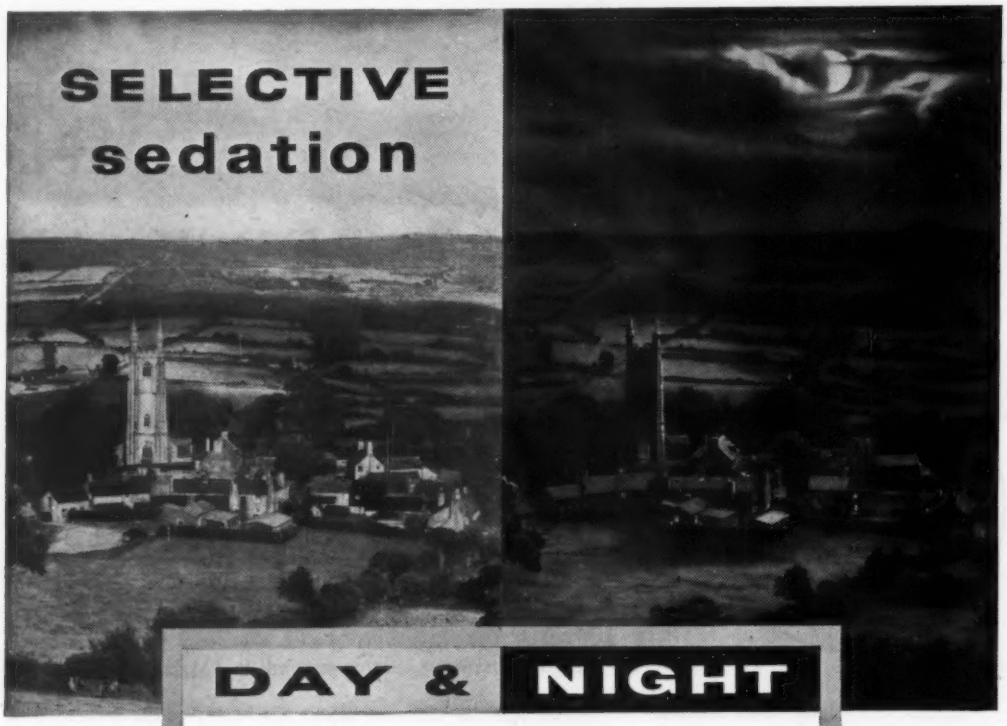

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26

RENAL EXCRETION OF WATER AND SALT *

E. B. VERNEY
M.A., M.B. Cantab., F.R.C.P., F.R.S.
SHEILD PROFESSOR OF PHARMACOLOGY IN THE UNIVERSITY OF CAMBRIDGE

(*concluded from page 1242*)

Excretion of Electrolytes

I come now to the question of whether or not this maintenance of near constancy in the " osmotic pressure " of the internal environment through the action of the antidiuretic hormone on water excretion is facilitated by an accompanying action on the excretion of electrolytes.

I have already mentioned that the inhibitory effect of posterior-pituitary extract on the rate of water excretion by the perfused isolated kidney of the dog is associated with an increase in the rate of chloride loss. The dose of extract needed to produce these effects is, however, far greater (200–500 times) than that needed to produce comparable degrees of decrease in urine flow during water diuresis in the living dog; and here the evidence about whether or not this decrease is associated with an increase in the rate of chloride excretion is conflicting. Dr. B. E. Andersson, Dr. D. A. Denton, and I therefore investigated this question by determining, in an established water-diuresis in the dog, the effects on chloride excretion of superimposing for a limited time an infusion of posterior-pituitary extract upon an infusion of sodium chloride at both low and high rates.

The preparation of the bitches for this investigation was similar to that previously described, but the method of urine collection was modified so that accurate serial measurements of the rate of chloride loss could be made.

The catheter was cut short near the vulva and connected by T-piece and rubber extension-tubing with a glass delivery-tube whose nozzle was 20 cm. below bladder level and emptied into a 10-ml. burette with tap, placed immediately over the collecting flask. To the side arm of the T-piece was attached a short piece of rubber tubing that was closed by a bull-dog clamp. Before the collection of the first sample of urine was begun, the bladder was drained, the clamp transferred to the extension tube, and 10 ml. of warm sterile redistilled water was injected by syringe into the bladder. The clamp was transferred back to the side-limb and the bladder redrained. This procedure was repeated twice, the complete return of the injected fluid being checked by means of the burette. As the last volume of distilled water was being injected a stop-watch was started; and, immediately after the bladder had been drained, the clamp was transferred to the catheter, the extension tube drained and washed through with 5 ml. of distilled water followed by air, and the clamp then replaced on the side-limb. Finally the walls of the burette were washed down with 5 ml. of distilled water, and a dry tared flask was placed below for the collection of the first sample of urine.

The periods of collection were about 10 minutes. The first was terminated by a repetition of the above-described process, a second stop-watch being started at the same time as the first was stopped. The periods thus followed continuously, and each was timed to the nearest second. The volumes of urine were determined by weighing each flask with its contents and subtracting therefrom the weight of the flask and the 40 ml. of distilled water used to wash the bladder, the collecting system, and the burette. The amount of chloride in each specimen was determined by Volhard's method.

For the intravenous infusions two syringes were used, and the plunger of each was propelled by a screw driven by a geared electric motor. Each syringe was filled with sterile liquid paraffin, and one was connected with the upper end of a glass bulb containing the sodium-chloride solution, the lower end being connected in turn with the infusing needle by means of polyethylene tubing and a short length of rubber tubing. The second syringe was connected by T-piece with two bulbs, of which one contained distilled water and the other posterior-pituitary extract suitably diluted with distilled water; and each in turn was connected by polyethylene tubing with a needle inserted into the rubber tube to which the needle infusing saline solution was attached. Thus, by clamping the connection between the syringe and one or other bulb, anti-diuretic hormone could be infused or withheld without altering the rate of infusion of saline solution and water. With the smaller input of sodium chloride the solution entering the vein was a little " hypotonic " (137 m*M*), and with the larger input it was strongly " hypertonic " (1·37 and 1·23 *M*). The rate of total fluid infusion, only 12·35 ml. per hr., remained constant throughout the experiment.

Four primary types of experiment were made after the test dose of water had been given by stomach-tube: (1) control experiments in which the weaker solution of sodium chloride was infused; (2) experiments in which posterior-pituitary extract was infused for 30 minutes during the infusion of the weaker solution of sodium chloride; (3) experiments in which the stronger solution of sodium chloride was infused; and (4) experiments in which posterior-pituitary extract was infused for 30 minutes during the infusion of the stronger solution of sodium chloride.

(1) The results of a control experiment are given in fig. 12. There was no certain change in the rate of chloride excretion over the 140 minutes of infusion, the rate varying between 9·3 and 12·7 μEq. a minute and being the same when the urine flow was 3·0 ml. a minute as at the end, when the urine flow was 0·68 ml. a minute—i.e., with the gradual subsidence of diuresis the concentration of chloride in the urine changed from 3·1 to 13·7 mEq. per litre without significant change in the rate of chloride loss.

Now, if we assume that the total body-water is 70% of the animal's weight, that the original tonicity of this fluid is equivalent to that of a solution of NaCl containing 150 mEq. of chloride per litre, and that the osmotic effects of the water and chloride balances are evenly distributed therein, the course of the changing tonicity of the total body-water during the experiment can readily be plotted. This has been done at the bottom of fig. 12.

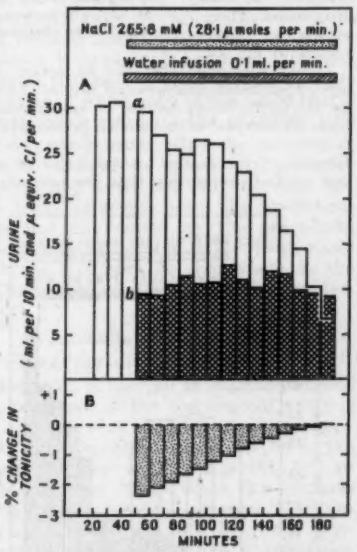
NaCl 265·8 mM (28·1 μmoles per min.)
Water infusion 0·1 ml. per min.
A
a
b
B
URINE (ml. per 10 min. and μ equiv. Cl′ per min.)
% CHANGE IN TONICITY
MINUTES
20 40 60 80 100 120 140 160 180

Fig. 12.—" Tess," Wt. 15.0 kg.: water 400 ml. was given by stomach-tube at zero time; A, rate of urine flow (*a*) and of Cl′ excretion (*b*); B, percentage change in tonicity of total-water phase, assumed to have an initial value of 10,500 ml. and a tonicity corresponding to that of a solution of NaCl containing 150 mEq. of Cl′ per litre; changes in tonicity were calculated from water and chloride balances (Andersson, Denton, and Verney, unpublished observations).

In view of the findings already alluded to in connection with the release of the anti-diuretic hormone by a local rise in the osmotic pressure of the carotid blood, it is of interest that, in the present experiment, the urine flow began its consistently maintained fall when the osmotic pressure of the total body-water had risen to 1% below the " isotonic " level, and that the diuresis had subsided just when this level was reached.

(2) In the second series of experiments posterior-pituitary extract was infused for 30 minutes during the course of three experiments like the one just described, and in none was there any certain change in the rate of chloride loss that could be related to the giving and withholding of the extract and the large changes in urine flow that resulted from them. The doses of extract used were either 2 mU followed by the infusion of 1·2 μU per sec. or 5 mU followed by the infusion of 6 μU per sec. The results of one such experiment are given in fig. 13.

(3) In the third series of experiments the stronger solution of sodium chloride was infused, and here the rate of chloride excretion increased apparently linearly during the infusion and while the diuresis was maintained. Between 60 and 70 minutes after the infusion was begun and between 100 and 110 minutes after the test dose (400 ml.) of water had been given by stomach-tube, the urine flow of 2·5–3·5 ml. a minute rapidly fell to 0·1–0·5 ml. a minute, and with this fall the rate of chloride loss, after a temporary decrease, became accelerated. These effects are illustrated in fig. 14.

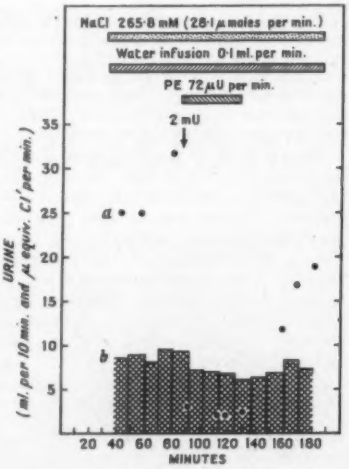
NaCl 265·8 mM (28·1 μ moles per min.)
Water infusion 0·1 ml. per min.
PE 72 μU per min.
2 mU
a
b
URINE (ml. per 10 min. and μ equiv. Cl′ per min.)
MINUTES

Fig. 13—"Tess": water 400 ml. was given by stomach-tube at zero time; plotting points, rate of urine flow; histograms, excretion of Cl′; calculations similar to those made in fig. 12 showed that, at end of experiment, total-water phase was hypotonic to extent of 1.1% (Andersson, Denton, and Verney, unpublished observations).

It was presumed that the inhibition of urine flow and its associated acceleration in the rate of chloride loss were caused by the endogenous release of antidiuretic hormone resulting from the increase in the osmotic pressure of the blood; and it was found that, when the course of the percentage change in the tonicity of the animal's total water phase was determined—and on the assumption that the osmotic effects of the water and chloride balances were evenly distributed therein—the increasing osmotic pressure was passing through the "isotonic" level (150 mEq. per litre) just when the urine flow began its precipitate fall. This is illustrated by the graph at the bottom of fig. 14.

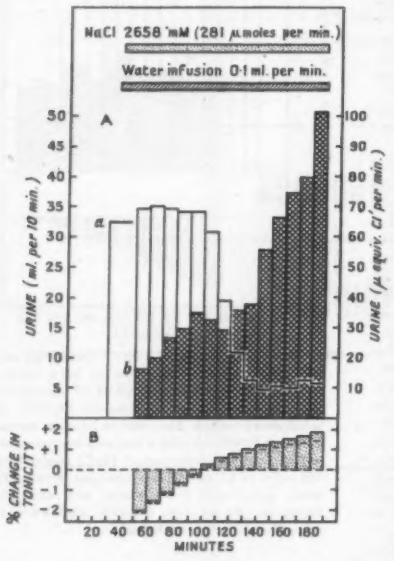

Fig. 14—"Tess" water 400 ml. was given by stomach-tube at zero time. A, rate of urine flow (a) and of Cl′ excretion (b); B, percentage change in mean tonicity of total-water phase (see legend to fig. 12): interrupted line, percentage change calculated for chloride loss of double the actual; precipitate fall in urine flow begins as mean tonicity of total-water phase is passing through "isotonic" level, and during inhibition of urine flow rate of chloride loss is accelerated (Andersson, Denton, and Verney, unpublished observations).

It was of interest, therefore, to see whether both of these effects (the precipitate fall in urine flow and its associated acceleration in the rate of chloride loss) could be antedated by the infusion of posterior-pituitary extract before the expected time of their onset.

(4) We made six experiments of this nature, and in all of them infusion of the extract caused an acceleration in the rate of chloride excretion; and the subsequent recovery of urine flow was associated with an absolute fall in this rate. After this, in three of the experiments, the final inhibition of urine flow supervened, presumably from endogenously released hormone, and the rate of chloride loss then increased again. The results of one such experiment are given in fig. 15. The increase in chloride output during the pituitary inhibition of urine flow, the decrease during the secondary diuresis, and the increase during the final subsidence of diuresis are well seen. Here again, as on some previous occasions, the percentage change in tonicity of the total body-water during the course of the experiment has been plotted at the bottom of the figure: the final fall in urine flow began just about the time when the rising tonicity of the animal as a whole was passing through the "isotonic" level. The preceding pituitary antidiuresis and increased chloride loss took place when the mean tonicity of the total body-water phase was about 1% below the "resting isotonic" value.

The results of our experiments on the effects of the antidiuretic hormone on water and chloride loss show that, under the simple hypotonic conditions of excessive intake of water, the antidiuretic action of the hormone is unaccompanied by any change in chloride excretion, and that this holds during the natural subsidence of diuresis due to the endogenous release of the hormone as the osmotic pressure of the total body-fluid approaches the prediuretic "isotonic" level.

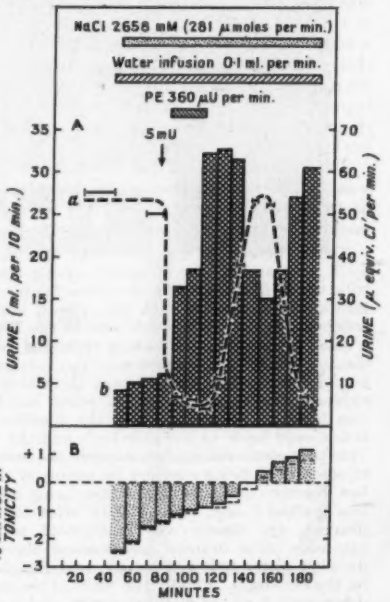

Fig. 15—"Tess": water 400 ml. was given by stomach-tube at zero time; A, rate of urine flow (a) interrupted line; horizontal lines give actual measurements) and of Cl′ excretion (b); B, percentage change in mean tonicity of total-water phase (see legend to fig. 14); antidiuretic action of posterior-pituitary extract is accompanied by increased rate of chloride loss; as urine flow recovers, rate of chloride loss falls and then increases again with final inhibition of urine flow; this final inhibition begins as mean tonicity of total-water phase is passing through "isotonic" level; pituitary inhibition of urine flow and increased rate of chloride loss occur when tonicity of total-water phase is still about 1% below "isotonic" level (Andersson, Denton, and Verney, unpublished observations).

When, however, a rapidly accumulating positive balance of sodium and chloride ions is imposed on these conditions, the antidiuretic action of the hormone is associated with an increased excretion of chloride, and this holds during the final subsidence of diuresis due to the endogenous release of the hormone.

The perfusion conditions in the kidney that enable the hormone to have this effect on chloride excretion need experimental defining; but it is of interest that conditions may be imposed in the living animal such that the chloride-excretion response of its kidney to the antidiuretic hormone is similar to that of the isolated kidney perfused by a heart-lung preparation.†

† See addendum 1.

Site of Osmoreceptors

Where, then, are the osmoreceptors, through whose functioning the secretion of the antidiuretic hormone is physiologically determined, situated? They are not in the carotid sinus. Moreover, in a bitch that showed close similarity between the responses to like injections into the two common carotid arteries, this similarity persisted after division of one carotid nerve and so belied the attractive hypothesis that the carotid body, innervated by the glossopharyngeal nerve through its carotid branch, was engaged in "tasting" (so to say) the osmotic properties of the internal environment.

Ligation of the internal carotid artery, however, definitely affected the responses from injections into the "common" carotid trunk. In the bitch whose residual response after removal of the posterior lobe of the pituitary gland is shown in fig. 6, and which was consistently giving such responses, it was found that, after the internal carotid had been tied near its origin, the injections which were previously effective now failed to cause any inhibition whatever.

Moreover, in a bitch with intact neurohypophysis, ligation of one internal carotid abolished for a time the large inhibitions of urine flow that were previously obtained from intracarotid injections on the same side. Later, responses were elicited, but erratically so. This was thought to be due to the short arterial anastomosis between the maxillary artery and the ophthalmic branch of the internal carotid artery; and it was predicted that, if one internal carotid artery were tied intradurally in the living animal, the responses to a raised osmotic pressure in the common-carotid blood of the same side would be permanently suppressed.

Since the receptors lie somewhere in the vascular bed normally supplied by the internal carotid artery, and since the responses to intracarotid injections or infusions are, so far as one can judge from the completely unconcerned attitude of the animal, devoid of perceptive accompaniment, the most reasonable working hypothesis to adopt would seemingly be one that places the receptors somewhere in the hypothalamus.

Their linkage with the neurohypophysis justifies a careful histological scrutiny of its main nucleus; and I have there observed vesicles with features that appear to be admirably suited to an osmoreceptive function:

In each of four dogs that were anæsthetised with chloralose and had their brains thereupon fixed by perfusion with formaldehyde-saline solution these structures were identified in both divisions of the supraoptic nucleus, whereas in one dog that had died some hours before the pituitary region was exsected and fixed in formaldehyde-saline solution, none were seen. This is evidence against their being artefacts.

In one of these four dogs serial sections of the whole supraoptic region were made, and those of the nuclei were drawn at a magnification of × 87. The roughly spherical nature of the vesicles was thereby disclosed, and their maximal anteroposterior and transverse diameters were computed. There were 89 such vesicles; they varied a good deal in size, and their average diameter was about 60 μ.

In another and much larger dog, whose posterior pituitary lobe had been removed fifty-one days before fixation of the brain, only 32 vesicles were counted. They do not contain fat. I suggested (Verney 1947) that, if indeed they were tiny osmometers, they might be functioning by having attached to them as stretch receptors the dendrites of neighbouring supraoptic cytons, increases in the osmotic pressure of their highly vascular environment being thereby transmuted into electrical wave messages to the secretory endings of the supraoptico-hypophyseal tracts.

More recently Jewell (1953) made a more extensive histological study of these vesicles and showed that they are intracellular structures formed in the cytons of the nuclear clumps of neurones and have axon processes which presumably join the supraoptico-hypophyseal tracts.

I emphasise, however, that the ascription of an osmotic function to these structures is at present little more than speculative, and that the only sure means of localising the osmoreceptors is to compare the effects of a rise in the osmotic pressure of the carotid blood before, with those after, intradural ligation of one or more of the branches of the internal carotid artery, and thereafter to map the cerebral distribution of the blood that had been carrying an osmotic stimulus to the brain.

For this latter purpose Jewell and Verney (1952) use two coloured dispersions. When all needed observations on the animal have been made, these dispersions are infused, one into each carotid, under exactly the same conditions as when hypertonic solutions were being infused, and the animal is suddenly killed by the intracardiac injection of chloroform through an anæsthetised intercostal space before the dispersions have had time to recirculate. The brain is then fixed, embedded in celloidin, and serially sectioned; and from examination of the sections the cerebral distributions of the two carotid bloods can be determined. We have been able to show that, as predicted, intradural ligation of an internal carotid artery completely or almost completely suppresses the responses that were being previously obtained from a rise in the osmotic pressure of the common-carotid blood of the same side.

Further, the posterior lobe of the pituitary gland has been excluded from being the site of the osmoreceptors. This has emerged from the fact that the posterior lobe commonly receives its blood-supply from one or other internal carotid artery as it runs forward in the cavernous sinus; and in such animals osmotic responses have been obtained from infusions of hypertonic solutions into each of the common carotid trunks. In other words, osmotic responses may be obtained when none of the blood carrying the osmotic stimulus is reaching the posterior lobe of the pituitary.

Furthermore, in an animal in which the posterior communicating artery had been tied on one side, the osmotic responses from infusions into the ipsilateral carotid trunk were not diminished by the procedure. The results of experiments that have so far been made suggest, then, that the receptors lie somewhere in the prosencephalon. There, for the time being, the problem of localisation rests.‡

Addenda

1—RENAL EXCRETION OF ELECTROLYTES

I have since found that, if the fall in plasma-chloride resulting from the absorption of the test dose of water is "corrected" by the intravenous injection of an appropriate dose of sodium chloride, the antidiuresis from the subsequently infused extract is accompanied by an increased rate of chloride loss. Thus, when this increase takes place, although the "osmotic pressure" of the extracellular fluid may be abnormally low, the concentration of chloride ions is higher than it otherwise would be. Now, in the early experiments with the heart-lung-kidney preparation the serum-chloride level was abnormally high. In view of the information obtained from the living animal it will therefore be of importance now to return to the heart-lung-kidney preparation to assess the relative significance of the plasma concentrations of sodium and chloride ions, on the one hand, and of the perfusion pressure, on the other, as determinants of the antidiuretic hormone's role in augmenting the renal excretion of these electrolytes.

Moreover when, under the experimental conditions outlined here, the rate of chloride loss increases, as a result of either infusion of extract or endogenous release of hormone, the rate of sodium loss increases as well. The parallelism, however, is not strict; and there are many tempting experimental possibilities, both under the conditions of perfusion of isolated organs and under those surgically attainable in the living animal, of

‡ See addendum 2.

exposing and giving physiological definition to the factors governing the release of the mineral corticoids and to the circumstances of their action on the renal excretion of electrolytes.

2—LOCALISATION OF OSMORECEPTORS

The results of work on the localisation of the osmoreceptors have since been published in detail (Jewell and Verney 1957). Of prosencephalic structures, the greater part of the telencephalon has been eliminated from being the receptor site by demonstrating the ipsilateral retention of responses after total hemispherectomy. Furthermore the heavy degenerative cell-loss in all thalamic nuclei of the hemispherectomised animal, excluding some cell groups of the midline, substantiated earlier indications that the receptors were not in the dorsal diencephalon. Alternative and equally compelling evidence for this conclusion was obtained from experiments in which carotid blood was directly excluded from the thalamus. Such exclusion was attained by tying the posterior communicating and occipital arteries of one side and either the middle cerebral or the anterior cerebral artery. It was also attained in an experiment in which the left internal carotid artery was tied intradurally, this leading to a redistribution of blood from the circle of Willis such that the thalamus was supplied entirely from vertebral sources. It was thus deprived of any right-carotid blood, although osmotic responses to intracarotid infusions on this side were retained.

The collation of the several evidences that I have just summarised led to the inference that the osmoreceptors are situated somewhere in the anterior hypothalamus or preoptic areas. This was the only region of the brain which had invariably been supplied by that carotid artery from which osmotic responses were obtained when hypertonic solutions were infused into it.

An interesting support for the conclusion that the receptors lie in this region of the brain came from an animal in which the right internal carotid artery was tied intradurally. Before the ligation big responses were obtained to infusions into the right carotid artery and small responses to infusions into the left. After the right internal carotid artery had been tied, the responses to right-sided infusions vanished, but those to left-sided infusions became very much larger. When, later, the cerebral distributions of the two carotid bloods were determined with the coloured suspensions, it was found that left carotid blood was not only supplying the left anterior hypothalamus but also had trespassed across the midline to supply this very region on the right side as well.

Now, this osmoreceptive zone, of a volume of about 100 c. mm., is supplied from the internal carotid artery, the anterior and middle cerebral, and the posterior communicating arteries by tiny branches that arise in the immediate neighbourhood of the carotid trifurcation. If, then, these three branches were tied, each some 3 or 4 mm. from its origin, one would expect osmotic responses to be retained on that side since the osmotic stimulus would be carried just to that part of the brain where the receptors lie.

Two experiments of this nature were made, and in each instance responses to ipsilateral carotid infusions were completely absent after operation. This was a sobering experience, but it was in part allayed by necropsy findings:

In the first animal a cyst had appeared in the ipsilateral anterior hypothalamus, involving the whole of the dorsal region and sending a tongue to the floor of the tuber cinereum through the posterior division of the supraoptic nucleus. The position of the cyst, and the striking denudation of cells in the remaining hypothalamic nuclei would adequately explain the postoperative disappearance of responses to ipsilateral intracarotid infusions.

In the second animal, however, the hypothalamus was intact, although, as predicted, the whole of the anterior hypothalamic region on the operated side carried ipsilateral carotid blood and had therefore been receiving an osmotic stimulus in the carotid-infusion experiments; but a large cyst had appeared in the ipsilateral thalamus and had destroyed all the anterior and medial thalamic nuclei, having spread right up to the midline and caused degeneration of the thalamic paraventricular nucleus.

Now, in the hemispherectomised animal, in which, it will be remembered, responses to ipsilateral carotid infusions had been retained, the heavy degenerative cell loss in the thalamus was coextensive with the cystic and degenerative destruction of thalamic nuclei in the animal now under consideration, except that, in the hemispherectomised animal, the thalamic paraventricular nucleus and its connections with the hypothalamus had been preserved.

The present evidence, therefore, leads to the conclusion that the osmoreceptors are in the anterior hypothalamic region, but that their functioning depends on nervous connexions with the thalamic paraventricular nucleus. This nucleus lies ventromedial to the stria medullaris (the stria is visible by the naked eye) and extends from the coronal level of the optic chiasma to that of the posterior commissure; and it will be of interest to know whether destruction of this nucleus is followed by a quantitative change in the osmotic responses to ipsilateral carotid infusions. The nucleus can be surgically exposed through the parietal cortex at anterior thalamic levels, and Dr. F. Howarth and I are now engaged in a specific inquiry on the status of this nucleus in the osmoreceptive process. It follows from what has been said that, although the tiny vesicles which I described ten years ago in the supraoptic nuclei lie within the osmoreceptive zone, there is not yet any evidence that they mediate the osmotic release of antidiuretic hormone.

I wish to express my thanks to the council of the Royal Society and to the editorial boards of the *Journal of Experimental Physiology* and the *Irish Journal of Medical Science* for permission to reproduce certain material from their publications.

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". . . As Lord Horder once said, an address in Harley Street is not really a higher medical qualification, and it is curious how this medical enclave developed—Harley Street, Wimpole Street and a few neighbouring streets. The development is quite recent: when I came to London in 1920 there were 330 doctors in Harley Street—in 1900 there had been only 157. By 1950 the number in Harley Street was 798, with another 580 in the neighbouring streets, or 1378 altogether. Last year, 1956, there were 796 doctors practising in Harley Street, but there was a total of 1450 when one included Wimpole Street, Devonshire Place, Welbeck Street, Queen Anne Street and Portland Place. So that private practice among consultants appears to be going up, not down."—R. SCOTT STEVENSON, *Trans. Coll. Physcns Philad.* 1957, **25**, 87.

DIETARY FAT AND CHOLESTEROL METABOLISM

FÆCAL ELIMINATION OF BILE ACIDS AND OTHER LIPIDS

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IN studying the dietary factors which influence the serum-cholesterol level several workers (Groen et al. 1952, Kinsell et al. 1952, Ahrens et al. 1954, Bronte-Stewart et al. 1956) have found that the quality of the ingested fat is as important as its quantity. In general, many saturated fats of either animal or vegetable origin raise the serum-cholesterol level, and some highly unsaturated fats (oils) from either marine or vegetable sources tend to lower it. Fats with an intermediate degree of saturation have little or no effect on the serum-cholesterol level (Ahrens et al. 1957). Hydrogenation may convert some natural oils into cholesterol-increasing fats (Bronte-Stewart et al. 1956).

Because of the possible therapeutic implications of these observations, particularly in the management of atherosclerosis, more information is needed about the properties of dietary fats and their effects during long periods. We have therefore fed certain saturated and unsaturated fats to human beings for as much as sixty days; they have been fed separately and together; in some cases, the oils have been heated to simulate domestic cooking. In this communication we are concerned with correlating the action of these fats on the serum-cholesterol level with the fæcal elimination of fat, neutral sterols, and, in particular, bile acids.

Subjects, Diets and Procedures

The investigations were all made in a metabolism ward with the help of nurses trained in metabolic work. The subjects were ten Bantu and Cape Coloured men. Some had the residue of previous accident or disease; others were transferred from the general ward, where they had been treated for more recent disease (table I). While they were in the metabolism ward, no active disease was detected in any of the men by routine clinical examination; all had normal blood-counts, erythrocyte-sedimentation rates, urine analyses, serum-protein and blood-urea levels, liver-function tests (thymol and zinc turbidity), chest radiographs, electrocardiograms, and blood Wassermann reactions. No pathogenic organisms were present in their stools.

These men were all destitute, and during their sojourn in the metabolism ward steps were taken for their social and physical rehabilitation. Their physical activity was minimal.

Initially each man was fed a basal, low-fat diet consisting of maize meal, stamped maize (corn grits), white bread, black tea, sugar, and syrup, supplemented with 60 g. of casein and with 'Multivitamin' tablets. Minor variations in the constitution of the basal diet were made to suit the individual or the exigencies of the experiment; these are indicated in table I. Subjects 4–10 were given, in addition, 200 g. each of pumpkin (*Cucurbita maxima*) and squash (*Cucurbita* var., gem squash) daily. The basal diet was fed for at least a week before the true "basal period" of observation was started; it was given unchanged throughout the experiments, and trial substances were administered either as supplements or as isocaloric substitutes for sugar and syrup.

Dietary Fats

The fats studied included crude and refined sunflower-seed oil, cotton-seed oil, and hydrogenated coconut fat. The iodine value and the "sterol" content * of each batch of fat were determined as follows:

	Iodine value	*"Sterol" content (mg. per 100 ml.)*
Sunflower-seed oil crude)	136	681
" " " (refined) batch IV ..	138	..
" " " " batch V ..	135	..
" " " " batch VII ..	135	751
Cotton-seed oil (refined)	107	322
Hydrogenated coconut fat	6	303

The oils were usually administered raw, in divided doses. In one experiment, however, the sunflower-seed oil was heated in an open aluminium pot at 210°C for two hours; it was allowed to cool and was fed to the men as usual. The hydrogenated coconut fat was melted and either drunk or lightly fried with bread. These substances were taken without complaint by all except subject 1, who complained of distension and produced loose stools when on sunflower-seed oil (see below).

Collection of Specimens

Blood was taken for determining the cholesterol level before breakfast at about two-day intervals and at the end of each feeding period.

All stools were stored in a refrigerator. In subjects 4–10, regular evacuation was facilitated by the inclusion of squash and pumpkin in the basal diet. The daily stools of subjects 1–3 were pooled at various intervals, and samples were analysed for neutral sterols and total fat. In subjects 4–6, each 24-hour collection was weighed separately, and samples of each specimen were taken for determining dry weight, total fat, and neutral sterols. The results were subsequently expressed as mean figures for five-day periods. In addition, samples

* The term "sterol" is used here to indicate the Liebermann-Burchard chromogens of the unsaponifiable portion of the fat.

TABLE I—MATERIAL OF INVESTIGATION

Subject no.	Age (yr.)	Race	Basic diet			Clinical history
			Calories	Fat (g.)	Protein (g.)	
1	54	Bantu	2500	9	93	Admitted with pellagra and bacillary and amœbic dysentery, treatment completed 4 months before this study
2	30	Cape coloured	1800	6	87	Neurosyphilis with minimal sequelæ 3 months after treatment
3	22	Bantu	2500	9	93	Psychoneurosis, physically fit on admission
4	21	Cape coloured	2000	8	87	Admitted for rehabilitation after hæmorrhage 3 months previously from vascular malformation in mid-brain
5	57	Cape coloured	2000	8	87	Syphilitic aneurysm of thoracic aorta; symptomless since treatment 1 year previously
6	19	Bantu	2000	8	87	Schistosomiasis, no symptoms after antimony treatment completed 1 week before metabolic study
7	34	Bantu	2500	8	85	Extensive plantar warts, otherwise fit on admission
8	28	Bantu	2500	8	85	Residual hemiparesis after cerebrovascular accident 3 months previously
9	25	Bantu	2500	8	85	Acute encephalitis 2 months previously, with residual aphasia and mental deterioration
10	25	Bantu	2500	8	85	Flexion contractures of both arms after extensive burns 18 months previously

TABLE II—EFFECTS OF HYDROGENATED COCONUT FAT AND SUNFLOWER-SEED OIL FED SEPARATELY ON SERUM-CHOLESTEROL LEVEL

Subject no.	Serum-cholesterol (mg. per 100 ml.)			
	Period I: mean basal level* (10 days)	Period II: hydrogenated coconut fat 100 g. daily (12–15 days)	Period III: sunflower-seed oil 100 g. daily (12–15 days)	Period IV: hydrogenated coconut fat 100 g. daily (12 days)
7	86	105	56	..
8	156	259	139	..
9	124	..	93	163
10	113	..	86	147
Mean	119	168 (periods II and IV)	93	..

* Mean of four readings; all other figures are of serum-cholesterol levels at end of each feeding period.

were taken daily and combined and homogenised every five days for the determination of bile acids. In subjects 7–10 three-day collections of stools were initially combined and homogenised; the dry weight, total fat, neutral sterols, and bile-acids were determined for each three-day pool.

Analytical Procedures

Serum-cholesterol and β-lipoprotein-cholesterol were estimated by the method of Abell et al. (1952) modified by Anderson and Keys (1956). Fæcal neutral sterols (this includes the Liebermann-Burchard-reacting sterols only) were estimated by the same method. Iodine values of the dietary fats were determined by the macro-Wijs technique (A.O.C.S. official method Cd. 1–2). Fæcal fat was measured by the method of Van de Kamer et al. (1949). The dietary fat was calculated from the data of Fox and Golberg (1944) and checked by analysis of spot samples. Total bile acids in the fæces were measured by the method of Lewis (1957).

Results

EFFECTS OF DIFFERENT FATS ON SERUM-CHOLESTEROL LEVEL

The effects of different dietary fats on the serum-cholesterol level were determined in these ten men.

Fats Fed Separately for Short Periods

In subjects 7–10, after a basal period of twelve days, 100 g. of either sunflower-seed oil or hydrogenated coconut fat was substituted isocalorically for sugar in the diet for twelve to fifteen days. Then the fat was substituted for the oil, or vice versa, and fed for a further twelve days. The results are shown in table II and figs. 1–4. It will be seen that a substantial rise of the serum-cholesterol level above its basal value was produced by the hydrogenated coconut fat both when it was fed immediately after the

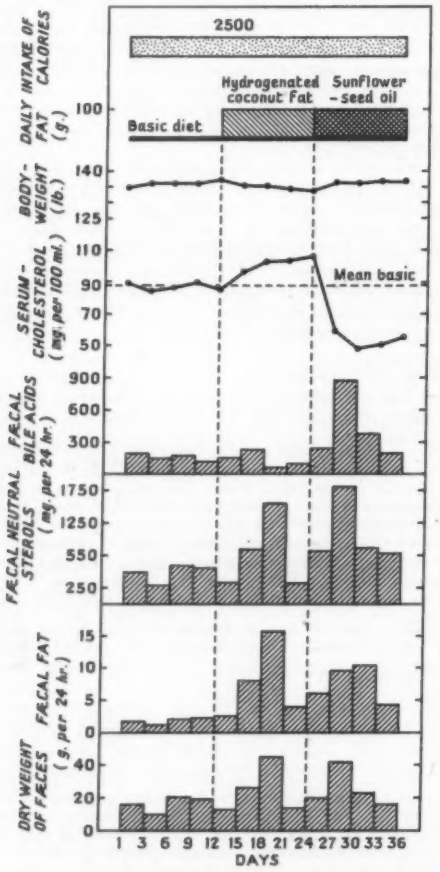
2500
Hydrogenated coconut Fat
Sunflower-seed oil
Basic diet
DAILY INTAKE OF CALORIES
FAT (g.)
BODY-WEIGHT (lb.)
SERUM-CHOLESTEROL (mg. per 100 ml.)
Mean basic
FÆCAL BILE ACIDS (mg. per 24 hr.)
FÆCAL NEUTRAL STEROLS (mg. per 24 hr.)
FÆCAL FAT (g. per 24 hr.)
DRY WEIGHT OF FÆCES
1 3 6 9 12 15 18 21 24 27 30 33 36
DAYS

Fig. 1—Subject 7: rise in serum-cholesterol level during treatment with hydrogenated coconut fat was accompanied by increase in total fæcal fat, fæcal neutral sterols, and dry weight of fæces. Decrease in fæcal bile acids was not significant. On feeding sunflower-seed oil however, there was a striking increase in fæcal bile acids but only slight increases in the other fæcal constituents.

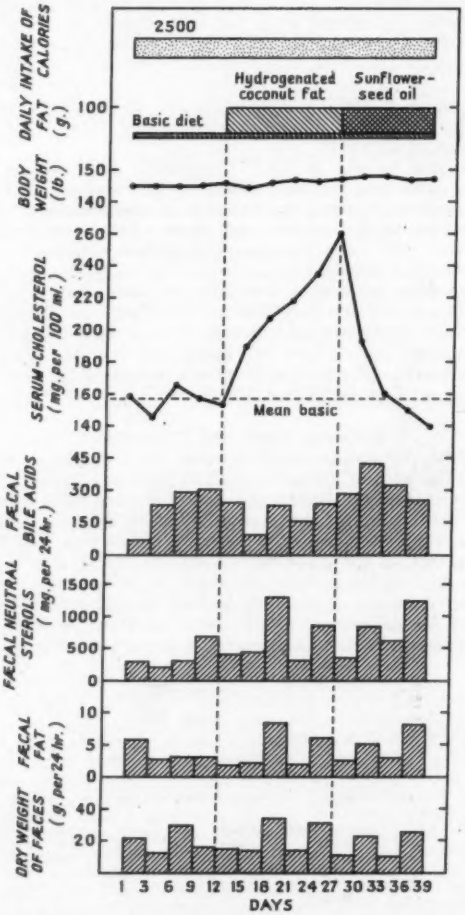
2500
Hydrogenated coconut Fat
Sunflower-seed oil
Basic diet
DAILY INTAKE OF CALORIES
FAT (g.)
BODY WEIGHT (lb.)
SERUM-CHOLESTEROL (mg. per 100 ml.)
Mean basic
FÆCAL BILE ACIDS (mg. per 24 hr.)
FÆCAL NEUTRAL STEROLS (mg. per 24 hr.)
FÆCAL FAT (g. per 24 hr.)
DRY WEIGHT OF FÆCES
1 3 6 9 12 15 18 21 24 27 30 33 36 39
DAYS

Fig. 2—Subject 8: sharp rise in serum-cholesterol level during treatment with hydrogenated coconut fat was promptly reversed by substitution of sunflower-seed oil. Changes in fæcal lipids are similar to those in fig. 1.

basal period and when it was substituted for sunflower-seed oil. Similarly, sunflower-seed oil lowered the serum-cholesterol level below its basal value both after the basal diet and after the hydrogenated coconut fat. The basal serum-cholesterol level in these four men was usually very low; the effect of the sunflower-seed oil was therefore all the more striking.

Fats Fed for Longer Periods

Subject 2 (fig. 5) was given 100 g. of crude sunflower-seed oil daily for thirty-four days in addition to his basal diet. The fall in the serum-cholesterol level was prompt and sustained. When the same amount of cotton-seed oil was substituted for sunflower-seed oil for a similar period, the serum-cholesterol level rose until it was very little below the mean basal value. A final substitution of hydrogenated coconut fat promptly raised the serum-cholesterol level still further.

In subject 1 (fig. 6) the effects of feeding equal amounts of sunflower-seed oil and hydrogenated coconut fat were again compared. While he was having sunflower-seed oil, the serum-cholesterol level was about 100 mg. per 100 ml. lower than it was during the fifty-eight days that he was having hydrogenated coconut fat. There was no significant difference between the effect of crude and refined sunflower-seed oil. In this man, as in subject 2, the cholesterol in the β-lipoprotein closely followed the trend of the total serum-cholesterol.

Saturated and Unsaturated Fats Fed Together

In subjects 4, 5, and 6, after ten days' basal diet, the addition of 75 g. of hydrogenated coconut fat—i.e., a calorie increment of 675—led to a sharp rise in the serum-cholesterol level (table III). After ten days of this régime the diet was further supplemented by 75 g. of heated sunflower-seed oil for fifteen days and by the raw oil for the next five days. During the latter twenty days the intake of calories was 3350 daily, and all three men gained weight. The rising trend of the serum-cholesterol level was halted and reversed, but the basal value was not reached. When raw oil was substituted for the heated oil, the serum-cholesterol level did not change in subject 4, rose slightly in subject 5, and fell slightly in subject 6. When the sunflower-seed oil was withheld, but the coconut fat was still given, the serum-cholesterol level rose again to its former high value. Fig. 7 is a representative illustration of this experiment.

A similar experiment was made on subject 3 (fig. 8). The fats were fed for longer periods, and the basal diet was supplemented by 100-g. quantities of fat. During the thirty days that sunflower-seed oil was fed in addition to the hydrogenated coconut fat, the serum-cholesterol level fell to basal values; it returned to its former height when the sunflower-seed oil was withdrawn.

EFFECTS OF DIFFERENT FATS ON FÆCAL EXCRETION OF LIPIDS

Fæcal Excretion of Fat

In subject 2 (fig. 5) it was noted that, when crude sunflower-seed oil was added to the basal diet, the fall in serum-cholesterol-level was accompanied by an initial increase in his fæcal fat. This increase was not maintained: after ten days his fat-absorption was within the

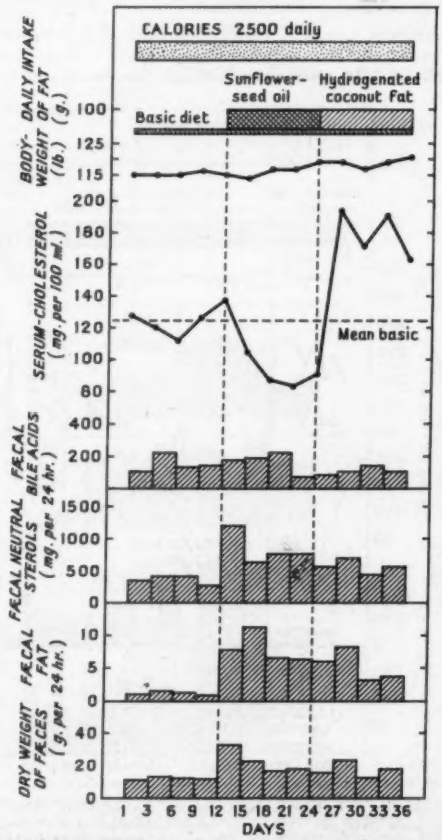
CALORIES 2500 daily
Basic diet
Sunflower-seed oil
Hydrogenated coconut Fat
BODY-WEIGHT (lb.)
DAILY INTAKE OF FAT (g.)
SERUM-CHOLESTEROL (mg. per 100 ml.)
Mean basic
FÆCAL BILE ACIDS (mg. per 24 hr.)
FÆCAL NEUTRAL STEROLS (mg. per 24 hr.)
FÆCAL FAT (g. per 24 hr.)
DRY WEIGHT OF FÆCES (g. per 24 hr.)
1 3 6 9 12 15 18 21 24 27 30 33 36
DAYS

Fig. 3—Subject 9: sunflower-seed oil was fed before hydrogenated coconut fat and was not so well absorbed as hydrogenated coconut fat; no great change in fæcal excretion of bile acids.

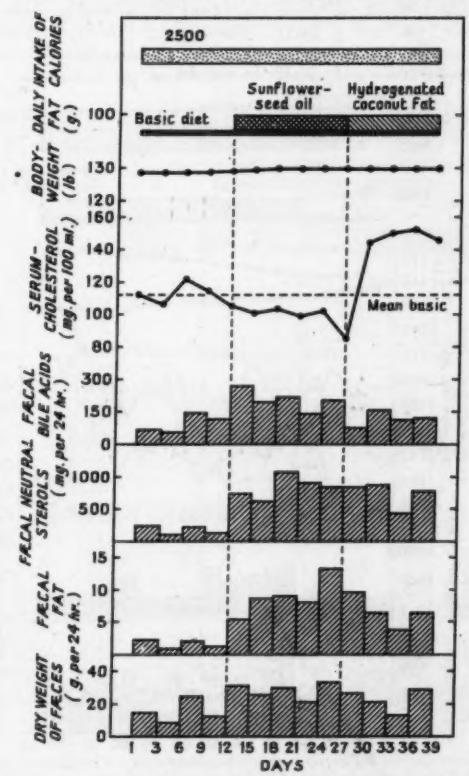
2500
Basic diet
Sunflower-seed oil
Hydrogenated coconut Fat
DAILY INTAKE OF CALORIES
FAT (g.)
BODY-WEIGHT (lb.)
SERUM-CHOLESTEROL (mg. per 100 ml.)
Mean basic
FÆCAL BILE ACIDS (mg. per 24 hr.)
FÆCAL NEUTRAL STEROLS (mg. per 24 hr.)
FÆCAL FAT (g. per 24 hr.)
DRY WEIGHT OF FÆCES (g. per 24 hr.)
1 3 6 9 12 15 18 21 24 27 30 33 36 39
DAYS

Fig. 4—Subject 10: introduction of sunflower-seed oil into basal diet lowered serum-cholesterol level and increased fæcal excretion of lipids. When hydrogenated coconut fat was substituted for sunflower-seed oil serum-cholesterol level rose sharply, fæcal excretion of bile acids decreased towards basal level, but changes in the other fæcal lipids were slight.

TABLE III—EFFECTS OF HYDROGENATED COCONUT FAT FED ALONE AND TOGETHER WITH HEATED OR RAW SUNFLOWER-SEED OIL ON SERUM-CHOLESTEROL LEVEL

Subject no.	Serum-cholesterol (mg. per 100 ml.)				
	Period I: mean basal level* (10 days)	Period II: hydrogenated coconut fat 75 g. daily (10 days)	Period III: hydrogenated coconut fat 75 g. daily + heated sunflower-seed oil 75 g. daily (15 days)	Period IV: hydrogenated coconut fat 75 g. daily + raw sunflower-seed oil 75 g. daily (5 days)	Period V: hydrogenated coconut fat 75 g. daily (10 days)
4	129	173	150	148	167
5	131	178	162	168	196
6	78	106	98	91	120
Mean	113	152	137	136	161

* Mean of three readings. All other readings are of the serum-cholesterol at the end of each feeding period.

normal limit of 93% (French 1955) and his weight progressively increased. Subject 1 (fig. 6), however, complained of distension and passed large stools throughout the period in which he was given sunflower-seed oil. Much fat was present in his stools, and his fat-absorption was persistently abnormal. He did not lose weight. Reduction of his very large intake of calories and the substitution of refined for crude sunflower-seed oil did not correct the abnormality. When hydrogenated coconut fat was substituted for the oil, the excretion of fæcal fat returned to normal. Other men absorbed the same batches of oil normally. Subject 3 (fig. 8) showed some increase in fæcal fat when his intake of fat was increased to more than 200 g. daily. Throughout the experiment, however, his fat-absorption remained within normal limits and he gained nearly 20 lb. in weight.

The results in subjects 4–10 are shown in tables IV and V and figs. 1–4 and 7. In summary, fat-absorption was essentially normal in all these men; 75 g. of hydrogenated coconut fat alone was no better absorbed than 75 g. of hydrogenated coconut fat plus 75 g. of sunflower-seed oil; the absorption of 100 g. of hydrogenated coconut fat was slightly more complete than that of sunflower-seed oil.

Fæcal Excretion of Neutral Sterols

The Liebermann-Burchard-reacting neutral sterols of the fæces were routinely measured in all cases. Figs. 1–8 indicate that the amount of these sterols in the fæces generally followed the trend of the total fæcal fat. The different effects of hydrogenated coconut fat and sunflower-seed oil on the amount of neutral sterols in the fæces of subjects 7–10 are shown in table VI and figs. 1–4. It will be seen that the addition of fat to the diet increased the fæcal excretion of neutral sterol; this effect was greater with sunflower-seed oil than with hydrogenated coconut fat. Table VI shows that these changes in the excretion of neutral sterol paralleled those of the total excretion of fat.

In subjects 4–6 the effects of hydrogenated coconut fat alone and with sunflower-seed oil on the fæcal excretion of neutral sterols were studied; the results are summarised in table VII and fig. 7. More neutral sterol was present in the fæces when the two fats were fed together than when hydrogenated coconut fat was fed alone. Comparison with table V again shows a general correlation of the excretion of neutral sterol with that of total fat.

Fæcal Excretion of Bile Acids

In subjects 7, 8, and 10 the inclusion of hydrogenated coconut fat in the diet produced little change in the amount of bile acids excreted in the fæces, and the

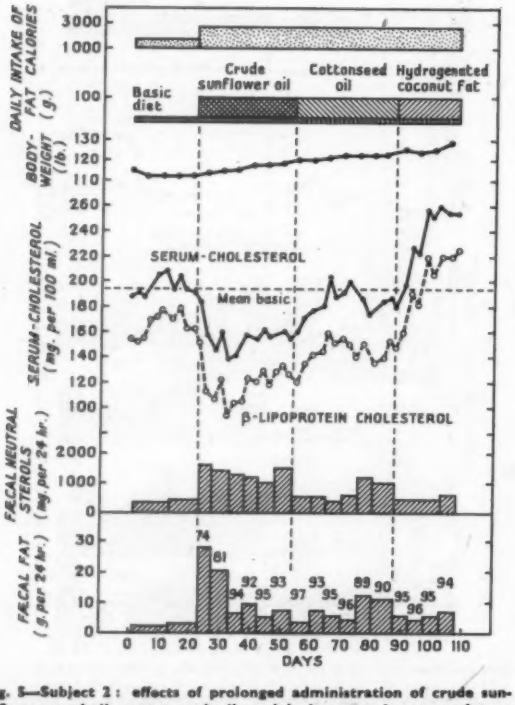

Fig. 5—Subject 2: effects of prolonged administration of crude sunflower seed-oil, cotton-seed oil, and hydrogenated coconut fat on serum-cholesterol level, total fæcal fat, and fæcal neutral sterols. Note transient increase in fæcal lipids when crude sunflower-seed oil is added to basal diet. Numerals above fæcal fat levels indicate percentage fat-absorption.

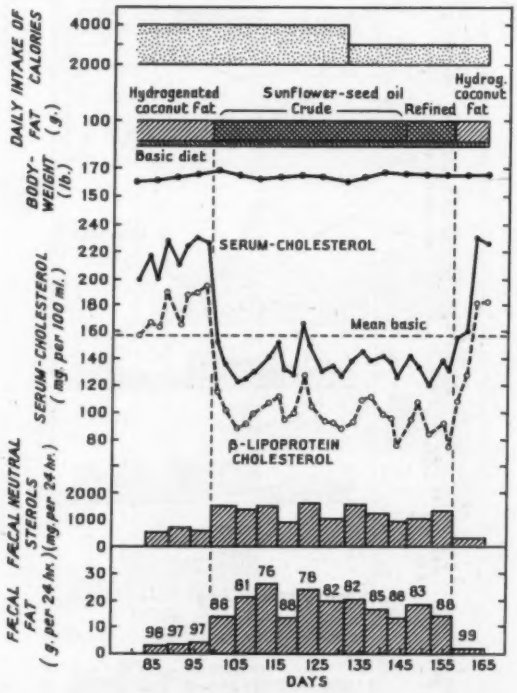

Fig. 6—Subject 1 had undergone another investigation before these data were obtained. Excessive fæcal excretion of fat throughout period of treatment with crude and refined sunflower-seed oil. "Mean basal serum-cholesterol level" was calculated from data recorded during an earlier period on basal diet without added fats.

serum-cholesterol level rose. When sunflower-seed oil was fed, however, the fæcal bile acids increased considerably, and the serum-cholesterol level fell (table VI and figs. 1, 2, and 4). In subject 9 the amount of fæcal bile acids did not change when sunflower-seed oil was fed, but it tended to decrease when hydrogenated coconut fat was fed (table VI and fig. 3).

In subjects 4–6 the addition of hydrogenated coconut fat to the basal diet produced little effect on the amount of fæcal bile acids. With the further addition of sunflower-seed oil, however, the fæcal excretion of bile acids was considerably increased (table V and fig. 7).

TABLE IV—EFFECTS OF HYDROGENATED COCONUT FAT AND SUNFLOWER-SEED OIL FED SEPARATELY ON FÆCAL EXCRETION OF FAT

Subject no.	Fæcal fat (g. per 24 hr.) Period I: basal diet 8 g. fat daily (12 days)	Period II: hydrogenated coconut fat 100 g. daily (12–15 days)	Period III: sunflower-seed oil 100 g. daily (12–15 days)	Period IV: hydrogenated coconut fat 100 g. daily (12 days)
7	1·7	7·4 (93·2 %)	7·4 (93·2 %)	..
8	2·6	3·9 (96·3 %)	5·1 (95·4 %)	..
9	1·1	..	7·9 (93·0 %)	5·4 (95·2 %)
10	1·8	..	8·3 (92·6 %)	6·3 (94·4 %)
Mean	1·8	5·7 (94·8 %) (periods II and IV)	7·2 (93·5 %)	..

Values given for fæcal fat are average daily figures for each period. Figures in parentheses are the apparent percentage fat-absorption. (No correction has been made for excretion of fat on basal diet.)

Discussion

EFFECTS OF DIFFERENT FATS ON SERUM-CHOLESTEROL LEVEL

These studies have confirmed and extended the observations previously made in this Department (Bronte-Stewart et al. 1956) and are consistent with reports from several other laboratories (Beveridge et al. 1956, Ahrens et al. 1957, Malmros and Wigand 1957). Thus it has been amply shown that serum-cholesterol levels can be lowered and kept low by the ingestion of certain fats.

Of special interest was the observation in subject 3 (fig. 8) that the addition of 100 g. of sunflower-seed oil to a diet already containing 100 g. of hydrogenated coconut fat reversed the effect of the latter on the serum-cholesterol level. In subjects 4–6 (table V, fig. 7) a similar but less striking reversal was observed. These data are important in relation to dietetics; they suggest that it may be possible to prescribe "cholesterol-decreasing" diets in which saturated fats are not rigorously restricted, provided that adequate amounts of unsaturated fats are included. Such a régime may prove more acceptable than the usual "fat-free" diet. Our experience with a group of ten European male volunteers supports this suggestion: in nine of these men supplementation of their regular diet with 50 g. of an oil daily produced and maintained significant falls of their serum-cholesterol levels during a six-month trial (Gordon et al. 1957).

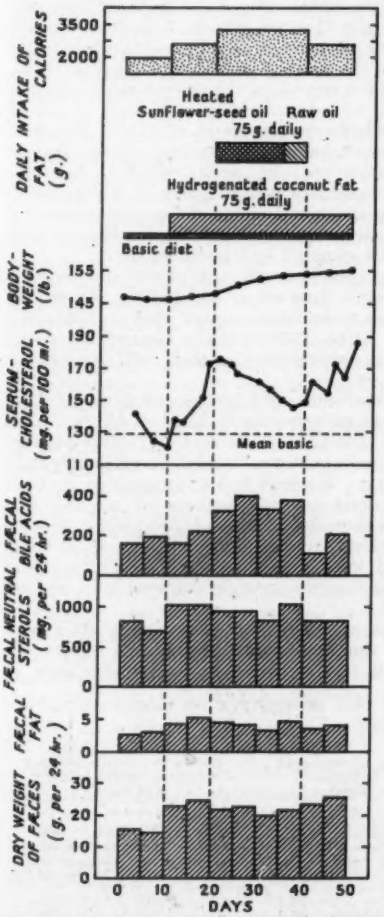

Fig. 7—Subject 4: addition of hydrogenated coconut fat to basal diet raised serum-cholesterol level sharply and increased total fæcal fat, fæcal neutral sterols, and dry weight of fæces; while fæcal excretion of bile acids was unchanged. Further addition of heated sunflower-seed oil reversed upward trend of serum-cholesterol level and increased fæcal bile acids, but other fæcal lipids did not change. Raw oil did not act differently from heated oil.

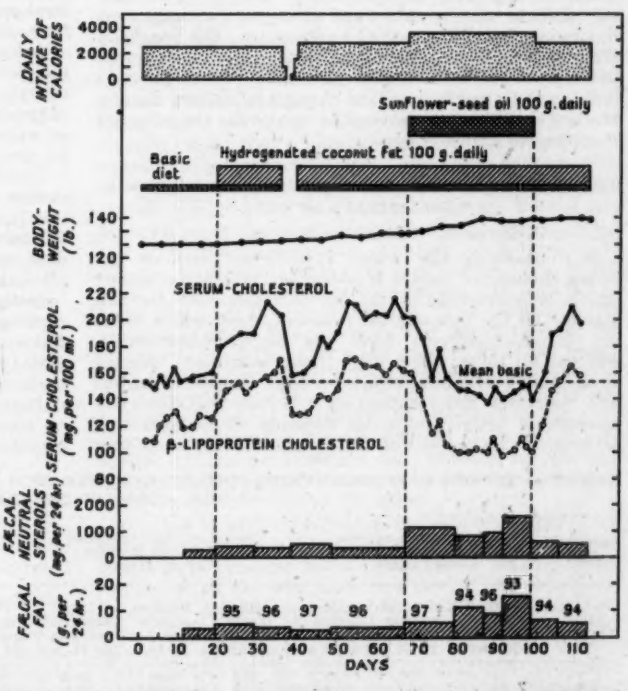

Fig. 8—Subject 3: hydrogenated coconut fat raised serum-cholesterol level. On 35th day the subject declined all solid food and subsisted on black tea and sugar for four days; during this period serum-cholesterol level returned to near basal value. When sunflower-seed oil was fed in addition to hydrogenated coconut fat, serum-cholesterol level fell to below basal value. Normal fat-absorption was maintained despite dietary load of 298 g. of fat daily.

TABLE V—EFFECTS OF HYDROGENATED COCONUT FAT FED ALONE AND WITH SUNFLOWER-SEED OIL ON FÆCAL EXCRETION OF FAT

Subject no.	Fæcal fat (g. per 24 hr.)			
	Period I: basal diet 8·25 fat g. daily (10 days)	Period II: hydrogenated coconut fat 75 g. daily (10 days)	Period III: hydrogenated coconut fat 75 g. daily + sunflower-seed oil 75 g. daily (20 days)	Period IV: hydrogenated coconut fat 75 g. daily (10 days)
4	2·8	4·7 (94·3%)	4·3 (97·4%)	3·8 (95·3%)
5	1·5	3·6 (95·7%)	8·7 (94·9%)	5·1 (93·7%)
6	3·8	3·9 (95·3%)	7·1 (95·4%)	3·6 (95·7%)
Mean	2·7	4·1 (95·1%)	6·7 (95·9%)	4·2 (94·9%)

Values given for fæcal fat are average daily figures for each period. The figures in parentheses are the apparent percentage fat-absorption. (See legend to table IV.)

The effect of domestic cooking on the activity of dietary fats may also have dietetic significance but has received little attention. Crampton et al. (1951) and Kaunitz et al. (1955) have shown that heating makes natural oils toxic to rats. In their experiments, however, the oils were heated at 80°C for 50–300 hours (Kaunitz et al. 1955) and 275° for twelve hours (Crampton et al. 1951)—i.e., under conditions which have little resemblance to conventional domestic practice. Our limited data suggest that, under conditions which simulate ordinary domestic cooking more closely, heating does not impair the effect of the sunflower-seed oil on the serum-cholesterol level.

Although it is clearly established that the serum-cholesterol level can be partly controlled by diet, we consider the general application of "cholesterol-decreasing" diets to the preventive and therapeutic management of coronary heart-disease to be premature. The beneficial effect of a low serum-cholesterol level on the development and regression of atherosclerosis remains to be proved; at this stage, therefore, radical changes in modern dietetic practice should not be advocated except for the purposes of controlled investigation.

MECHANISM OF ACTION OF DIFFERENT FATS ON SERUM-CHOLESTEROL LEVEL

Cholesterol-decreasing Factors in Natural Fats

In considering the action of different fats on the serum-cholesterol level it is important to define precisely which characteristic of the fat is responsible for this action. Of the fats studied thus far, those which lower the serum-cholesterol level are highly unsaturated, whereas all those which raise it are saturated. Ahrens et al. (1957), who have studied a large number of animal and vegetable fats, tentatively conclude that the cholesterogenic activity of a fat depends on its degree of saturation. In support of this conclusion they show that artificial saturation (hydrogenation) of corn and cotton-seed oils increases their cholesterogenic activity. Hydrogenation, however, produces more than mere saturation: isomerisation of the fatty acids may take place (Sreenivasan and Brown 1956), and this has been shown in animals to alter their physiological effects (Holman 1951). Sinclair (1956) and Kinsell et al. (1956) have suggested that cholesterol-decreasing action is directly related to the "essential fatty acid" content of an oil, and technical manipulation may impair this specific activity. This may explain the rising incidence of coronary heart-disease despite the increased availability of unsaturated fats (Hollingsworth et al. 1956, McCann and Trulson 1957), many of which have been processed commercially.

Keys et al. (1957), however, have found that, compared with sunflower-seed oil and sardine oil, the cholesterol-decreasing effect of corn oil is out of proportion to its degree of unsaturation and its content of essential fatty acids; they question the importance of both these qualities in determining the action of an oil. From experiments on animals Jones et al. (1957) postulate that the special virtue of corn oil resides in its unsaponifiable fraction rather than in the fatty acids, and Beveridge et al. (1957) have issued a preliminary note on a short-term dietary trial in which they claim to have "demonstrated unequivocally that the plasma cholesterol depressant effect of corn oil depends to a large extent upon its sterol content." Thus they differ from Ahrens et al. (1957), who could not reproduce the cholesterol-decreasing effect of corn oil by administering very large doses of β-sitosterol. Furthermore Ahrens et al. (1957) find that corn oil retains its cholesterol-decreasing potency despite a six-fold decrease of its unsaponifiable fraction. Similarly we have recently studied a man in whom 100 g. of pilchard oil significantly lowered the serum-cholesterol level, whereas feeding the unsaponifiable fraction derived from 100 g. of the same oil had no effect on it.

Some marine oils have considerable cholesterol-decreasing potency (Bronte-Stewart et al. 1956). These oils contain very little tocopherol (Lange 1950); hence the suggestion of Le Riche (1956) that the vitamin-E content of natural oils is responsible for their activity cannot be accepted.

Finally, our experience with hydrogenated coconut oil (iodine number 6) corresponds to that of Ahrens et al. (1957), who find that natural coconut oil (iodine number 9.7) raises the serum-cholesterol level more efficiently than does any other fat. Natural and hydrogenated coconut oil have the lowest iodine numbers of all the fats investigated, but they also have the highest saponification numbers—i.e., they are peculiarly rich in short-chain fatty acids—and the importance of the chain length of dietary fats in relation to serum-cholesterol level has yet to be elucidated.

It is obvious that much more investigation is needed to characterise the lipid component which effects the serum-cholesterol level. The practical importance of

TABLE VI—EFFECTS OF HYDROGENATED COCONUT AND SUNFLOWER-SEED OIL FED SEPARATELY ON FÆCAL EXCRETION OF BILE ACIDS AND NEUTRAL STEROLS

Subject no.	Period I: basal diet 8 g. fat daily (12 days)			Period II: hydrogenated coconut fat 100 g. daily (12–15 days)			Period III: sunflower-seed oil 100 g. daily (12–15 days)			Period IV: hydrogenated coconut fat 100 g. daily (12 days)		
	Bile acids (mg. per 24 hr.)	Neutral sterols (mg. per 24 hr.)	Dry weight of fæces (g. per 24 hr.)	Bile acids (mg. per 24 hr.)	Neutral sterols (mg. per 24 hr.)	Dry weight of fæces (g. per 24 hr.)	Bile acids (mg. per 24 hr.)	Neutral sterols (mg. per 24 hr.)	Dry weight of fæces (g. per 24 hr.)	Bile acids (mg. per 24 hr.)	Neutral sterols (mg. per 24 hr.)	Dry weight of fæces (g. per 24 hr.)
7	147	520	16·7	122	790	24·3	407	1080	25·4	..	..	..
8	220	380	19·1	188	650	20·9	314	750	16·5	..	..	..
9	110	370	12·8	..	..	..	113	840	22·7	74	570	17·5
10	92	210	15·3	..	..	..	205	850	28·4	125	710	22·5
Mean	142	390	15·9	127	680	21·3	258	880	23·2	..	..	..
				Periods I and IV								

These figures are the means of 24-hr. excretions calculated from 3-day collections of fæces.

TABLE VII—EFFECTS OF HYDROGENATED COCONUT FAT FED ALONE AND WITH SUNFLOWER-SEED OIL ON 24-HOUR FÆCAL EXCRETION OF BILE ACIDS AND NEUTRAL STEROLS

Subject no.	Period I: basal diet 8·3 g. fat daily (10 days)			Period II: hydrogenated coconut fat 75 g. daily (10 days)			Period III: hydrogenated coconut fat 75 g. daily + sunflower-seed oil 75 g. daily (20 days)			Period IV: hydrogenated coconut fat 75 g. daily (10 days)		
	Bile acids (mg. per 24 hr.)	Neutral sterols (mg. per 24 hr.)	Dry weight of fæces (g. per 24 hr.)	Bile acids (mg. per 24 hr.)	Neutral sterols (mg. per 24 hr.)	Dry weight of fæces (g. per 24 hr.)	Bile acids (mg. per 24 hr.)	Neutral sterols (mg. per 24 hr.)	Dry weight of fæces (g. per 24 hr.)	Bile acids (mg. per 24 hr.)	Neutral sterols (mg. per 24 hr.)	Dry weight of fæces (g. per 24 hr.)
4	170	750	14·5	188	1000	23·0	353	900	21·0	153	800	24·0
5	129	400	16·0	152	650	22·5	428	810	30·2	124	750	26·0
6	112	840	22·4	134	880	20·0	218	1270	32·5	132	750	24·0
Mean	128	663	17·6	158	843	21·6	333	993	27·9	136	766	23·7

These figures are the means of 24-hr. excretions calculated from 5-day collections of fæces.

such investigation in food technology and dietetics needs no emphasis.

Effects of Different Dietary Fats on Fæcal Fat

In the early stages of these investigations it was noticed that the sudden introduction of a large amount of fat into the basal diet occasionally produced transient diarrhœa (Bronte-Stewart et al. 1956). It was therefore possible that malabsorption was responsible for the fall in the serum-cholesterol level. In subject 2 (fig. 5) there was a temporary increase in the amount of fæcal fat when sunflower-seed oil was fed; his serum-cholesterol level, however, remained low even when his fat-absorption returned to normal.

Detailed studies in subjects 4–10 revealed no evidence of malabsorption. In subjects 7–10 (table IV; figs. 1–4) the slightly increased fæcal fat during treatment with sunflower-seed oil, compared with that during treatment with hydrogenated coconut fat, is of doubtful significance and cannot explain the striking changes in the serum-cholesterol level. In subjects 4–6 (table V) there was a mean increase in fæcal fat of 2·6 g. a day when the hydrogenated coconut fat was supplemented with sunflower-seed oil. Increasing the dietary fat generally increases the fæcal fat (Wollaeger et al. 1957); the increase in our men was probably a non-specific response to an increased dietary load and unlikely to be due to the quality of the ingested fat.

Subject 3 (fig. 8) was given the biggest dietary load of all: 100 g. each of hydrogenated coconut fat and sunflower-seed oil daily. He maintained a low serum-cholesterol level for a month while absorbing more than 180 g. of fat daily. Only subject 1 was persistently unable to absorb sunflower-seed oil normally. In fact, in a large number of clinical trials of sunflower-seed oil (Gordon and Brock unpublished) mild constipation was often observed, but diarrhœa was uncommon. Thus our experience confirms previous reports (Deuel 1954) that sunflower-seed oil is well absorbed. We conclude that its cholesterol-decreasing action is not due to malabsorption, and that the anomalous finding in subject 1 represents an individual intolerance to the oil.*

Effects of Different Fats on Fæcal Neutral Sterols and Bile Acids

Tracer studies in animals have established that the main end-products of cholesterol metabolism are excreted in the fæces. Cholesterol may be excreted as neutral sterol; this includes cholesterol itself and its closely related Liebermann-Burchard-reacting derivatives (Δ^7-cholestenol and dehydro-cholesterol); it also includes the saturated sterols coprostanol and dihydrocholesterol. Siperstein and Chaikoff (1955), however, have shown that the bile acids are the major end-product of cholesterol metabolism; in a man with a biliary fistula Siperstein and Murray (1955) found that 87% of ingested cholesterol was excreted as bile acid, mainly glycocholic acid.

Our data on sterol excretion are incomplete and include only the fæcal bile acids and the Liebermann-Burchard-reacting neutral sterols. The rest of the digitonin-precipitable neutral sterol fraction has not been measured; hence a complete picture of the differential action of saturated and unsaturated fats on sterol excretion cannot be drawn. The data show, however, that the excretion of Liebermann-Burchard-reacting neutral sterols does not reflect the changes in serum-cholesterol level but tends to follow quantitatively the total amount of fæcal fat. Probably the changes in the fæcal neutral sterols are partly due to quantitative changes in the dietary "sterols." Thus the increased excretion of neutral sterols during treatment with sunflower-seed oil may reflect the larger "sterol" content of this oil; it will be recalled that the sunflower-seed oil which we used contains twice as much "sterol" as does the hydrogenated coconut fat.

The excretion of bile acids, however, follows the fluctuations in the serum-cholesterol level closely: when the level rises during the ingestion of hydrogenated coconut fat, there is little change in the excretion of bile acids; when the level falls, however, the amount of fæcal bile acids is almost doubled. The changes in the amount of fæcal bile acids do not correlate with the amount of fæcal fat or with the dry weight of the fæces; they therefore represent a true increase in excretion of bile acids and do not indicate failure of reabsorption due to intestinal hurry. The increased excretion of bile acids during treatment with sunflower-seed oil is not a non-specific cholagogic action of fat; feeding an identical amount of hydrogenated coconut fat had an insignificant effect on the excretion of bile acids.

It must be emphasised that the amount of fæcal bile acids is not a direct measure of the total synthesis of bile acids in the liver but only represents the unresorbed residue of all the bile acids produced. The amount of fæcal bile acids is considerably modified by organisms (Bergström and Norman 1953) and possibly by other factors in their passage down the intestine. Despite these limitations, however, we consider the estimation of the fæcal bile acids to be a useful indication of cholesterol-bile acid turnover in man. Only by analyses of bile itself can a true estimate of the production of bile acids be obtained, but this limits investigation to patients with bile fistulæ, and it is unknown whether their digestion of lipids is normal.

* Since submitting this report for publication, we have seen the paper by L. Horlick and B. M. Craig (*Lancet*, 1957, ii, 566). They report that feeding with ethyl stearate fails to increase the serum-cholesterol level, and they further note that the absorption of this fat was only 60–70%. We have recently studied a healthy man in whom the administration of hydrogenated coconut fat failed to increase the serum-cholesterol level and in whom balance data showed malabsorption of this fat (70% absorbed). Lard, which he absorbed normally, increased his serum-cholesterol level. Hence we conclude that, in assessing the effect of a dietary fat on the serum-cholesterol level, its degree of absorption must be taken into account.

There is little evidence from experiments on animals to support the suggestion that the ingestion of unsaturated fat increases the production of bile acids. In rats Portman et al. (1955) increased the production of bile acids by feeding 5% cholesterol but not by feeding 15% vegetable fat. In rabbits, Mosbach et al. (1956) 12% triolein did not affect the excretion of sterols and bile acids; and 1% cholesterol in the diet increased the excretion of sterols but not of bile acids. A relationship between the serum-cholesterol level and the fæcal excretion of bile acids has, however, been shown in dogs: Abell et al. (1956) suggest that, in dogs, the development of hypothyroidism blocks the conversion of cholesterol to bile acids. Thus, when thiouracil is administered to dogs on a high-cholesterol intake, their serum-cholesterol level rises and fæcal bile acids decrease. In our subjects the ingestion of sunflower-seed oil was followed by a fall in the serum-cholesterol level and an increase in the fæcal bile acids. Possibly, therefore, one of the mechanisms whereby sunflower-seed oil influences the serum-cholesterol level is to promote the conversion of cholesterol to bile acids and hence its excretion from the body. Other mechanisms also may be important—e.g., the effects of different fats on the synthesis of cholecterol. These remain to be explored in man.

Summary

It is confirmed that the ingestion of an unsaturated fat, sunflower-seed oil, lowers the serum-cholesterol level. This effect has been maintained for sixty days. Hydrogenated coconut fat, fed under similar conditions, produced a sustained rise of the serum-cholesterol level.

In men fed large amounts of hydrogenated coconut fat the addition of an equal amount of sunflower-seed oil to the diet, with a corresponding increase in caloric intake, led to a substantial fall in the serum-cholesterol level.

When sunflower-seed oil was heated to a degree comparable with ordinary domestic cooking, there was no material change in its action on the serum-cholesterol level.

The introduction of sunflower-seed oil into the diet occasionally produced a transient excessive fæcal excretion of fat. In all but one man, however, normal fat-absorption was maintained for long periods with dietary loads of up to 200 g. daily.

The fall in the serum-cholesterol level due to sunflower-seed oil was accompanied by a slight increase of neutral sterols and a considerable increase of bile acids in the fæces. These changes can be interpreted as indicating that sunflower-seed oil promotes the katabolism and excretion of cholesterol.

This study was undertaken as part of the programme of the clinical nutrition research unit supported in the University of Cape Town by the South African Council for Scientific and Industrial Research. We acknowledge gratefully the financial assistance given by the South African Mutual Life Assurance Society; Irvin and Johnson, Ltd., of Cape Town; the South African Fish Oil Producers Association (Pty.) Ltd.; and the Archibald Read Richardson Research Fund. Technical and other assistance was given by Mr. G. F. J. Schoonraad and the staff of the metabolism ward: Miss J. Seward, B.SC., Miss E. Volks, B.SC., Miss C. Solms, Miss G. O. Martinius, B.SC., and Mr. R. Thompson. Finally, we wish to thank the directors and chief chemists of Messrs. Lever Bros. (S.A.) (Pty.) Ltd., and Marine Oil Refiners of Africa Ltd. for the supply of fats and oils and for other valuable assistance.

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AN EVALUATION OF SPUTUM EXAMINATION IN CHRONIC BRONCHITIS

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IN the bacteriological examination of sputum, difficulties may arise for several reasons. Firstly, the sputum may be contaminated by the bacterial flora of the mouth and pharynx (Mulder 1938): these may also overgrow, and thereby conceal, the pathogens derived from the bronchi. Secondly, because pathogens may be distributed irregularly in the sputum, culture of a small sample may not disclose their presence (May 1952). Thirdly, the use of special media is necessary, for some bacteria may otherwise escape detection because of their more exacting growth requirements. This is especially so in the case of *Hæmophilus influenzæ*.

Several methods have been recommended to overcome these difficulties.

Mulder (1938) described a method of washing the purulent flecks of sputum with three successive changes of saline solution to remove contaminating organisms from the throat. May (1952) found that multiple samples from the same specimen disclosed more pathogens than did single samples. Rawlings (1953) utilised this information and devised a method for homogenising sputum by enzymatic digestion with 1% pancreatin. Allibone et al. (1956), however, maintain that, providing a sufficiently large sample is cultured, satisfactory results can be obtained without digestion or washing of the specimen.

Because sputum examination is unreliable, attempts have been made to obtain material from the bronchi by direct aspiration, usually at bronchoscopy (Allison et al. 1943, Benstead 1950, Bergman et al. 1955, Tunevall and Wassermann 1956). However, even bronchial aspirates are liable to contamination

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Fig. 1—Apparatus for bronchial swabs.

by throat organisms (Bergman et al. 1955, Tunevall and Wassermann 1956), presumably introduced from the pharynx by the bronchoscope.

We have devised a method of direct swabbing of the bronchi which avoids aspiration and has been found to give reliable results. This method has been used to assess the bacterial flora in patients with and without chronic infection of the bronchi. By comparing these results with those obtained from sputum culture, we have attempted to evaluate the methods of bacteriological examination of the sputum.

The Patients and the Methods

69 patients were investigated by simultaneous culture of bronchial swabs, sputum, and throat-swabs. From the history, clinical features, and bronchoscopic findings, they fell into two groups. Group 1 contained 42 patients who had no history of chronic productive cough, and the appearances at bronchoscopy were normal. At the time of investigation they could produce small quantities of sputum. Group 2 contained 27 patients with a history of chronic productive cough of over a year's duration, with exacerbations associated with fever and an increase of pus in the sputum. Bronchoscopy revealed that 8 of these had distortion or obstruction of bronchi, usually associated with bronchial carcinoma. 5 others had bronchiectasis and the remaining 14 had uncomplicated chronic mucopurulent bronchitis.

TABLE I—POTENTIAL PATHOGENS IN 42 PATIENTS WITH NORMAL BRONCHI (GROUP 1)

Site	*H. influenzæ*	Pneumococci	Coliforms	β. hæmolytic streptococci	Total
Throat ..	5	17	5	6	33
Sputum ..	3	14	3	4	24
Bronchi ..	0	0	0	0	0*

* No other organisms were found in the bronchi.

Bronchoscopy

In all cases bronchoscopy was carried out by the same surgeon (L. L. B.).

Under general anæsthesia the bronchoscope is passed and a special polythene swab-carrier (fig. 1) is introduced. This consists of a metal rod with a serrated end to which sterile cotton-wool is attached immediately before use. The rod lies within a polythene tube, to the end of which is attached a protective metal cup.

The swab-carrier is passed down the bronchoscope with the swab retracted. The swab is advanced for sampling and again retracted before withdrawal from the bronchoscope.

Swabs were taken in most cases from the carina, the main bronchi, and the bronchi of the upper, middle, and lower lobes. Earlier in the investigation bronchial aspirate was also obtained, but this method proved unsatisfactory because of contamination by throat organisms, and was abandoned.

Sputum

An early-morning specimen was obtained on the day of bronchoscopy. This was expectorated into a universal container or carton and transported to the laboratory without delay. Throat-swabs were also examined.

Bacteriological Technique

Sterile saline solution was added to the sputum in the universal container and gently agitated. The saline was poured off into another sterile container and subsequently cultured. The sputum was then tipped into a sterile petri dish, and cultures were made from the purulent and mucoid portions. Films were also prepared at this stage on microscope slides and stained by Gram, Giemsa, and Papanicolaou techniques. The sputum was then divided into two equal parts. One part was digested with 1% pancreatin (Rawlings 1953) and the other was subjected to mechanical shaking with glass beads.

All specimens were plated on the following media:

Two blood-agar plates, one being incubated aerobically and one anaerobically; a blood-agar plate containing gentian-violet (1 : 500,000) and incubated in 10% carbon dioxide; a chocolate agar plate (for the isolation of *H. influenzæ*); and a MacConkey plate.

TABLE II—POTENTIAL PATHOGENS IN 27 PATIENTS WITH VARIOUS BRONCHIAL LESIONS (GROUP 2)

Site	*H. influenzæ*	Pneumococci	Coliforms	β-hæmolytic streptococci	Total
Throat ..	8	8	2	2	20
Sputum ..	17	10	5	3	35
Bronchi ..	18	4	4	1	27†

† In 5 cases more than one pathogen was present in the bronchi; in 5 cases the bronchi were sterile.

Hæmophilus influenzæ were provisionally identified by their colonial appearance and by the Gram stain.

Suspicious colonies were obtained in pure growth and tested for their growth requirements by adding the growth factors to the chemically defined medium of Cohen and Wheeler (1946). Finally, agglutination tests were done with specific antisera.

Pneumococci were identified by bile solubility and sensitivity to optochin (Bowers and Jeffries 1955). Coliforms, including Friedländer's bacillus, paracolon bacilli, and *Proteus vulgaris*, were identified by conventional methods. Group-A hæmolytic streptococci were identified by their sensitivity to bacitracin (Maxted 1953).

Results

In 42 patients with no abnormality of the bronchial tree (group 1), swabs from this site were uniformly sterile (table I). Organisms commonly regarded as pathogens were, however, cultured from the sputum in 24 instances. The same organisms were invariably present in the throat.

Table II shows that organisms were found in the bronchi in many of the patients with lesions of the bronchial tree (group 2). *H. influenzæ* was the commonest organism, being present in 18 cases, followed by pneumococci, coliforms, and β-hæmolytic streptococci. In only 2

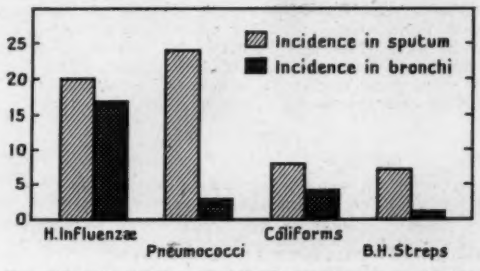

Fig. 2—53 patients with potential pathogens in sputum, showing proportion with organisms in the bronchi.

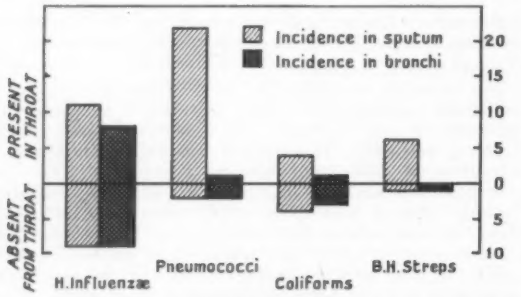

Fig. 3—Patients from fig. 2, grouped according to presence or absence of organisms in throat.

instances were organisms present in the bronchi but not recovered from the sputum. Organisms present in the sputum were not necessarily recovered from the bronchi, and this discrepancy was most marked in the case of pneumococci (fig. 2). There was a much closer degree of correlation between sputum and bronchial-swab culture when the organism was absent from the throat (fig. 3).

Discussion

It has come to be recognised that, of the wide variety of organisms found in sputum, only a small number are associated with bronchial infections. These are commonly referred to as bronchial pathogens or potential pathogens and include *H. influenzæ*, pneumococci, coliforms of various types including Friedländer's bacillus, β-hæmolytic streptococci, and *Staphylococcus aureus*, in decreasing order of importance (May 1954, Mulder 1956). Evidence for the pre-eminent position of *H. influenzæ* and pneumococci as the pathogens in chronic bronchitis has been derived from the high incidence of these organisms, singly or together, in sputum in this disease (Mulder 1952) and particularly at times when the sputum is purulent (Elmes et al. 1953, May 1953a). More direct evidence incriminating *H. influenzæ* in those cases with bronchiectasis has been obtained by cultures from bronchial aspirations (Allison et al. 1943).

The presence in the sputum of organisms known to be non-pathogenic throat commensals has generally been interpreted as nothing more than a reflection of unavoidable contamination with pharyngeal material during the process of expectoration. This view is supported by the frequency with which pharyngeal squames are seen in sputum samples on microscopy. Attempts to reduce such contamination by washing the flecks of sputum before culture are only partially successful (Bergman and Colldahl 1956), and this is not surprising since it is common to find an intimate degree of mixing of the pharyngeal and bronchial elements of sputum as shown by the occurrence of pharyngeal squames, often with adherent bacteria, bronchial epithelial cells and "dust" cells in close proximity within a single high-power field in smears of sputum (fig. 4). Therefore some contamination by pharyngeal material, including bacteria, is unavoidable. The extent of this contamination can be assessed by the finding of pharyngeal squames in the specimen.

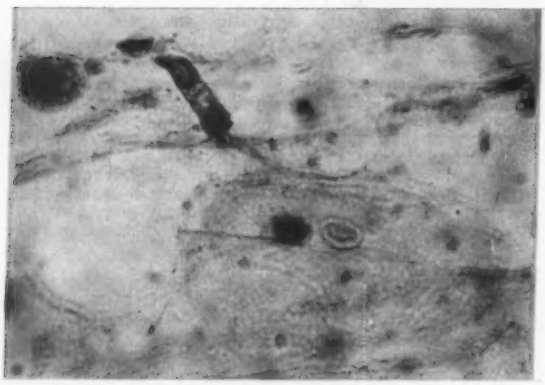

Fig. 4—Smear of sputum showing a pharyngeal squame adjacent to a bronchial epithelial cell and histiocyte (×1000).

In a significant proportion of people, pneumococci, *H. influenzæ* and the other bronchial pathogens are found in the nasopharynx unrelated to disease (Straker et al. 1939). Contamination of the sputum with these organisms, derived from the throat, was common both in patients with normal bronchi and in those with lesions of the bronchi who were expectorating true sputum (tables I and II). The resulting discrepancy between simultaneous sputum and bronchial cultures is apparent in fig. 2, especially in the case of the pneumococcus, which is found in 30–50% of normal throats. This discrepancy very largely disappears when the organism in question is absent from the throat at the time of sputum production (fig. 3). The finding of a potential pathogen in the sputum, when it is simultaneously absent from the throat-swab, thus assumes a much greater significance (fig. 3). We have found examination of a throat-swab useful as an adjunct to the culture of sputum in cases of chronic respiratory disease.

Clearly, the bronchial tree is normally sterile (table I), and the technique of bronchial swabbing is unlikely to give erroneous results due to contamination with throat flora provided care is taken during the procedure.

The reliability of bronchial swabbing in recovering organisms from the bronchi is impossible to assess in absolute terms, but is thought to be satisfactory in that *H. influenzæ*, which is a relatively delicate organism, was recovered from 18 out of 19 patients with chronic bronchitis, some of whom also had bronchiectasis. This high recovery-rate agrees with the expected prevalence of this organism in chronic mucopurulent bronchitis, as found in a large series of cases reported by Mulder (1940), and in cases of bronchiectasis by Allison et al. (1943).

The efficacy of the cultural methods we have used in the examination of sputum may be judged by considering how commonly pathogens were isolated from the sputum of patients with the organism in the bronchi. Of the 27 cases in which a pathogen was found by bronchial swabbing (table I), it was recovered from the sputum in 25.

Our findings regarding the incidence of pathogens in the bronchi in chronic mucopurulent bronchitis, with or without bronchiectasis, agree with those of Mulder (1956), May (1954) and Allibone et al. (1956) in emphasising that *H. influenzæ* is commonly present. We differ, however, from Mulder in that we find the additional presence of pneumococci in the bronchi to be relatively rare. Any contamination of sputum by throat flora would be liable to increase the apparent incidence of pneumococci in this disease as indicated above.

Summary

A technique is described for direct swabbing of the bronchi. It has been found to give satisfactory results.

By this method it has been confirmed that the bronchi are normally sterile in health.

By comparison of the cultural results from simultaneous examination of sputum, throat-swabs, and bronchial swabs, it has been shown that sputum is often contaminated from the throat by those organisms generally regarded as bronchial pathogens, and therefore may give an inaccurate indication of bronchial infection.

When the organism in question is absent from the throat, a closer correlation is obtained between the flora of the sputum and the flora of the bronchi.

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OBSERVATIONS ON THE GASTROŒSOPHAGEAL JUNCTION DURING SWALLOWING AND DRINKING

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IN the long debate on the mechanism of the gastro-œsophageal junction the presence or absence of a sphincter has been hotly contested. In 1954 Dornhorst et al. showed clearly that, when liquid barium is drunk off, it enters the stomach with no delay at the gastro-œsophageal junction. In 1956, however, Fyke et al. (1956) were able to demonstrate, in the resting state, a segment of raised intraluminal pressure, 2–3 cm. long, lying between the œsophageal and gastric pressures and higher than either. On swallowing, the pressure in this area fell, and the pressure barrier was temporarily abolished in the manner of a sphincter relaxing. This fall in pressure began 1·5–2·5 seconds after swallowing and lasted some 5 or 6 seconds until the peristaltic wave reached the gastroœsophageal junction. Although in this study the subjects were observed during "dry" swallowing, the results suggest that liquids are held up at the gastroœsophageal junction until the sphincter has opened.

These conflicting reports seemed hard to reconcile. The present investigation, using simultaneous cineradiography and pressure measurements, was designed to reinvestigate the problem by contrasting the events at the gastroœsophageal junction during the drinking of barium and during the swallowing of barium that had been previously held in the mouth. The events which have been analysed take place between the act of deglutition and the arrival of the peristaltic wave at the gastro-œsophageal junction.

The term "gastroœsophageal junction" denotes the area covering the lowest 3 cm. of the œsophageal tube and not the exact point of transition from tube to stomach.

Methods

The intraluminal pressures were measured indirectly through fine water-filled polyethylene tubes attached to Hansen capacitance manometers. Three tubes were used, each recording by a lateral hole cut so they were spaced 5 cm. apart. The distal part of the middle tube, beyond the recording orifice, was filled with mercury so that the exact position of this recording orifice could be seen radiographically.

The cineradiographic films were taken with a Marconi image intensifier at 16 frames per second. To keep the dose-rate as low as possible the fastest film available was used (Ilford H.P.S.) together with 4 mm. Al tube filtration. The dose received by each subject was about 5 r. The pressure recordings and cine film were synchronised by means of a solenoid which was placed at the edge of the X-ray field and closed and simultaneously marked the pressure tracing in response to a hand switch.

The observations were made on ten healthy medical students. The tubes were passed through the mouth and placed so that the middle tube was in the gastroœsophageal junction. This was recognised by the point of reversal of the inspiratory pressure swing and the increased amplitude of the respiratory pressure swing about this point. The barium swallow was filmed with the subject standing, in seven subjects in the right anterior oblique position and in three in the left oblique. In the first series of experiments the subjects were given either 20 or 40 ml. of fluid barium to hold in the mouth and after a pause of about 1 to 2 minutes were asked to swallow it. In the second series they were given in a cup the same volume of barium, which they were asked to drink in one gulp. Any pressure tracing showing that the subject had swallowed within 30 seconds of starting the experiment was discarded. There were seventeen satisfactory combined pressure and cine records of the first series and fourteen of the second available for analysis.

Analysis

In the pressure tracings the resting end expiratory pressure was taken as the baseline from which changes in pressure were measured. In the cine films the time was measured from the act of deglutition to the arrival of barium at the gastroœsophageal junction, the opening of the junction, the maximal width of the junctional lumen, and the emptying of the œsophagus. The sudden rise of intraœsophageal pressure was taken as the time of deglutition.

Results

Swallowing Barium

The general pattern seen in this series of experiments was that the barium streamed into the lower œsophagus and was held up at the gastroœsophageal junction, only passing into the stomach after some delay (fig. 1).

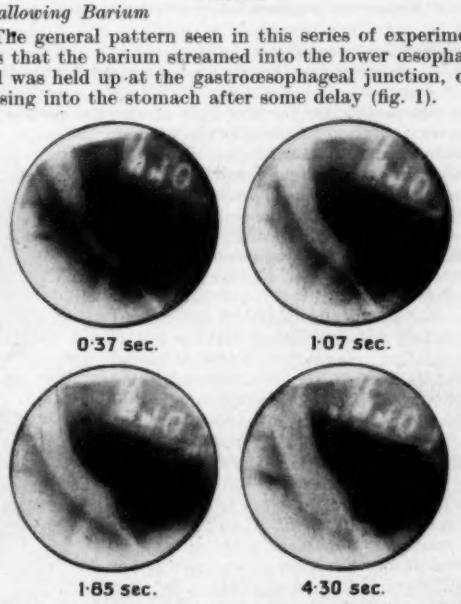

Fig. 1—Swallowing barium; right anterior oblique position. Timing of each frame after deglutition is indicated. Synchronising marker is at top right. At 0·37 sec. barium is seen reaching gastroœsophageal junction and is in contact with mercury-filled tube. At 1·07 sec. barium is still held up, and at 1·85 sec. frame is first showing barium passing through junction. At 4·30 sec. junctional lumen has reached its maximum.

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At the moment of swallowing there was an abrupt rise in pressure in the œsophagus, though barium did not reach the gastrocœsophageal junction until 0·8 seconds later (fig. 2). As the barium reached the junction, the mean œsophageal pressure, recorded 5 cm. above this level, was + 10 cm. water. The barium was held up at the gastrocœsophageal junction for an average delay of 1·4 seconds, and during this pause the pressure in the œsophagus remained fairly constant. In two of seventeen experiments in this series there was no delay in the passage of barium at the junction—i.e., barium flowed steadily from œsophagus to stomach in the interval between two frames, though the lumen of the junction was narrow.

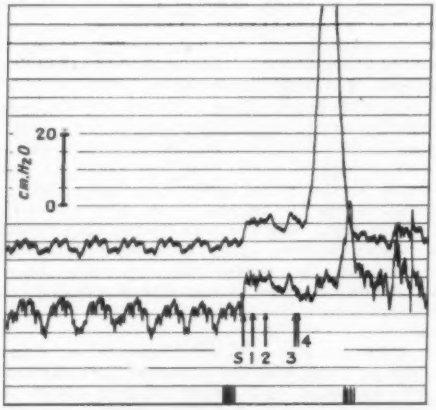

Fig. 2—Pressure during swallowing of barium synchronous with cine-films shown in fig. 1. Upper tracing from lower œsophagus, lower tracing from gastrocœsophageal junction immediately above point of reversal of inspiratory pressure swing. Marks at bottom of recording are synchronising signal. Time marker is in secs. S, act of swallowing; 1, arrival of barium at junction; 2, opening of junction; 3, junction maximally open; 4, all barium has left œsophagus. Note constant intraœsophageal pressure during hold-up of barium and that all these events take place before arrival of peristaltic wave.

Radiologically the point of hold-up showed some variation but was about the level of the shadow of the left leaf of the diaphragm. However, in the pressure recordings the point of hold-up was sharply localised to the point of reversal of the pressure swing with inspiration. The exact position of the recording orifice in the gastrocœsophageal junction could be seen as the top of the mercury filled part of the tube. When this was above the point of reversal of inspiratory pressure swing, with the result that a fall in pressure was recorded during inspiration, the top of the mercury-filled tube was within the held-up column of barium (figs. 1 and 2). Conversely, when the orifice was recording a rise of pressure during inspiration, the opaque tube was seen to be below the barium outline. The abrupt rise of pressure with swallowing was always present when the recording was made above the point of reversal of inspiratory pressure swing (fig. 2) but was always absent in recordings below it (fig. 3). In two experiments a biphasic pressure swing was recorded during inspiration, first positive and then negative, and in both these instances the abrupt rise of pressure on swallowing was present and the tip of the opaque tube was just in contact with the barium outline.

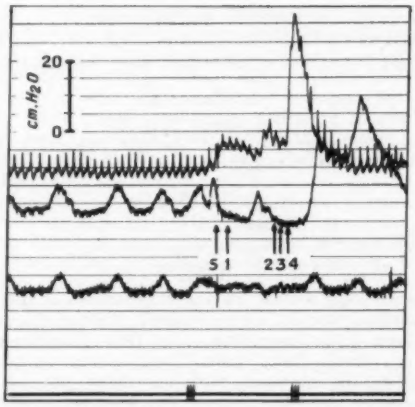

Fig. 3—Pressure during swallowing of barium. Upper tracing from lower œsophagus, middle tracing from junction below point of reversal of inspiratory pressure swing, lower tracing from stomach. S, act of swallowing; 1, arrival of barium at junction; 2, opening of junction; 3, junction maximally open; 4, all barium has left œsophagus. Note fall in pressure in junction after swallow.

A lumen appeared below the point of hold-up at a mean time of 2·2 seconds after deglutition. At first it was extremely narrow, but it gradually widened until it was only slightly less than that of the lower œsophagus. The length of this junctional segment could not be measured with any accuracy, because the barium column usually streamed from it into the stomach without altering the calibre; but it appeared to be about 2 cm. long. The lumen of this segment reached its maximum in a mean time of 3·9 seconds after deglutition. The pressure in this area, recorded below the point of hold-up, fell after deglutition in six out of ten experiments (fig. 3). This fall began about the time barium reached the junction; by the time the junctional lumen opened, the mean pressure was − 4 cm. water; and as the lumen reached its maximum the mean pressure was − 7 cm. water. During inspiration the lumen of the junctional segment

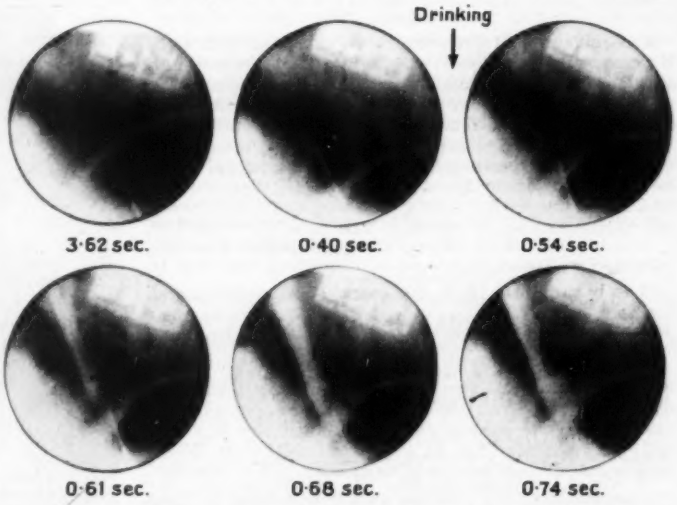

Fig. 4—Drinking barium; right anterior oblique position. At 3·62 sec. resting and expiratory position of diaphragm; at 0·40 sec. extent of diaphragmatic descent as cup is raised to lips. Next four frames show barium flowing through widely open junction without delay.

was suddenly obliterated, and it opened just as suddenly during expiration.

After the gastrocesophageal junction had opened maximally, the barium flowed rapidly through, and in every instance the œsophagus had completely emptied before the arrival of the peristaltic wave at the junction.

The œsophageal pressure usually began to fall after the opening of the junction, and it continued to fall as the œsophagus emptied. The gastric pressure remained unchanged after deglutition in most experiments.

Drinking Barium

The general pattern in this series was that the barium reached the lower œsophagus and passed without any delay through the junction into the stomach (fig. 4).

However, before the barium was drunk, a change in diaphragmatic position was observed. As the cup was raised to the lips, the diaphragm descended to the extent only seen during deep inspiration. Immediately before deglutition the diaphragm started to rise; hence, when barium was seen passing through the junction, the

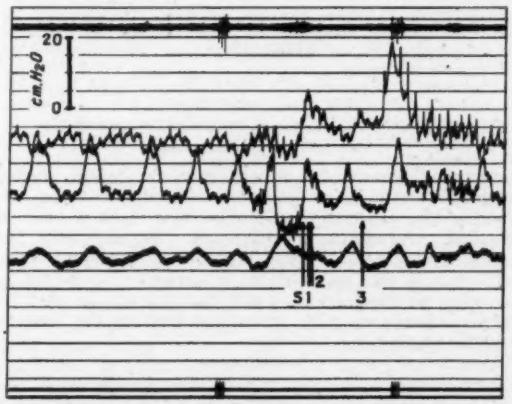

Fig. 5—Pressure during drinking of barium. Upper tracing from lower œsophagus, middle tracing from junction, lower tracing from stomach S, act of drinking; 1, barium passing through junction without delay; 2, junction maximally open; 3, all barium has left œsophagus. Note pressure changes before drinking, as cup is raised to lips.

diaphragm was about halfway back to the end expiratory position. This descent of the diaphragm was not accompanied by the well-marked pressure changes recorded during deep inspiration. The mean fall in intrathoracic pressure was only 2 cm. water more than that recorded during quiet inspiration, and similarly the mean rise in intra-abdominal pressure was only 1 cm. water above the value for quiet inspiration—whereas on deep inspiration these values are increased by about 8 cm. water. The intra-abdominal pressure had nearly returned to the end expiratory level by the time barium was seen passing through the junction.

The barium arrived at the gastrocesophageal junction in a mean time of 0·6 seconds. In ten out of the fourteen experiments the barium flowed into the stomach without any delay—i.e., in the interval between two frames. The mean delay for the whole group was only 0·1 seconds. As the barium arrived, the junctional lumen was either widely open or widened to its maximum with extreme rapidity. In three experiments the lumen of the junctional segment was maximally open as barium entered, and in two others the maximal lumen was present within 0·1 seconds. For the whole series the junctional lumen reached its maximal width in 1·1 seconds after deglutition. The barium passed swiftly through the junction and had left the œsophagus in a mean time of 3·3 seconds after deglutition.

TABLE I—MEAN TIME OF RADIOLOGICAL EVENTS AT THE GASTRO-ŒSOPHAGEAL JUNCTION AFTER DEGLUTITION

After	Barium arrives junction (sec.)	Opening of junction (sec.)	Lumen of junction attains maximum (sec.)	All barium passed through (sec.)	Delay of barium at junction (sec.)
Swallowing	0·8 ±0·1	2·2 ±0·3	3·9 ±0·4	5·9 ±0·3	1·4 ±0·4
Drinking	0·6 ±0·1	0·7 ±0·1	1·1 ±0·2	3·3 ±0·5	0·1 ±0·1

Values following ± sign are standard errors of means.

The intraœsophageal pressure, measured 5 cm. above the junction, showed an abrupt rise at the moment of deglutition, and the mean pressure as barium arrived at the junction was + 14 cm. was (fig. 5). After this the pressure fell so that when the lumen of the junctional segment was at its widest the mean pressure was + 11 cm. water. At the gastrocesophageal junction the preliminary descent of the diaphragm resulted in the recording orifice being above the diaphragm at the moment of deglutition, when an abrupt rise in pressure was recorded in every experiment. In most experiments, there was no change in pressure in the stomach after deglutition, but in a third of them a slight fall was recorded.

Comparison of Two Series

There was a considerable difference in the timing of the radiological events between swallowing and drinking barium (table I). However, the initial rise of pressure in the œsophagus was, on average, higher on drinking barium than on swallowing it, although by the time the lumen of the junction had reached its maximum the œsophageal pressures were similar in both groups (table II). This initial pressure head influenced the time of opening and the time taken for the lumen to reach its maximum; hence these events took place earlier if the initial pressure was sufficiently high. Even so, when the pressure was similar in both series, the junction usually opened earlier on drinking than on swallowing, and the widening of the lumen was clearly accomplished much earlier on drinking than on swallowing barium. Therefore, although the initial pressure head above the junction did play some part in the speed of its opening, this could not by itself explain the difference between the two series. There remained a distinct difference in the behaviour of the gastrocesophageal junction during swallowing and during drinking.

Discussion

These observations appear to resolve the conflicts between previous investigations, which showed either that a sphincter was present at the gastrocesophageal junction or that there was no evidence of one at all. The resolution lies in the difference between the physiology of swallowing and drinking.

The observations during the swallowing of barium show that there is a sphincteric mechanism under the control of deglutition. These findings confirm the results of Fyke et al. (1956). In particular the fall in pressure in the junctional segment after the act of deglutition is

TABLE II—MEAN PRESSURES IN LOWER ŒSOPHAGUS 5 CM. ABOVE GASTROŒSOPHAGEAL JUNCTION

After	Barium arrives at junction (cm. water)	Opening of junction (cm. water)	Maximum lumen of junction (cm. water)	All barium passed through (cm. water)
Swallowing	10 ±1·6	11 ±1·4	9 ±0·8	7 ±1·0
Drinking	14 ±1·1	14 ±1·1	11 ±1·1	6 ±1·5

Values following ± sign are standard errors of the means.

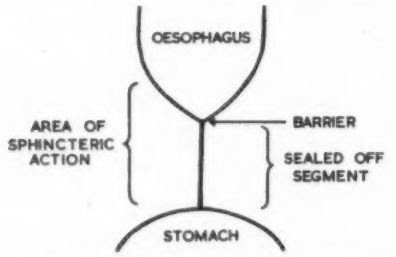

Fig. 6—Diagrammatic summary of functional components of gastro-œsophageal junction.

similar in timing and amplitude to their data. It is clear that the sphincter is not strong, because it can be forced open prematurely by a sufficiently high intraœsophageal pressure.

This sphincteric segment appears to be the lowest part of the œsophageal tube and about 2 cm. long. Also within the junctional area are the point where the flow of swallowed barium is arrested and the point where the inspiratory pressure swing reverses. These two points are identical in position and indicate a definite barrier. It is unlikely that this barrier coincides exactly with the proximal limit of the sphincteric area, because it has been shown that the point of reversal of inspiratory pressure swing usually lies in the middle of the band of high pressure; but there is considerable individual variation (Fyke et al. 1956). This suggests a sphincteric area within which is a barrier isolating the distal part, which we have described as the sphincteric segment, from the œsophagus (fig. 6).

The barrier is narrowly localised, because the inspiratory pressure swing usually reverses within 0·5 cm. (Dornhorst et al. 1954, Fyke et al. 1956). It seals off the sphincteric segment from changes in pressure in the œsophagus, and in this respect the segment resembles the gastroœsophageal vestibule described by Sanchez et al. (1953); but we have been unable to find any evidence of a vestibular structure.

The barrier is also the point of change from an intra-abdominal to an intrathoracic pattern of respiratory pressures, but it seems unlikely that it simply represents the level of the diaphragmatic hiatus. The hiatus is impossible to localise from radiographs without the aid of markers (Botha 1957), but it is certain that the diaphragmatic hiatus does not compress the œsophagus during expiration, whereas the barrier arrests the passage of barium throughout all phases of respiration. It therefore seems more likely that the barrier is a definite intrinsic structure.

The behaviour of the junctional segment during drinking confirms the findings of Dornhorst et al. (1954). Under these conditions there is no evidence of a sphincteric mechanism, and the junction appears wide open throughout. It seems reasonable to think that swallowing is the simpler action of the two, and that, in drinking, some additional factor comes into play to open the junction before the arrival of barium. Possibly this is a reflex inhibition of the sphincter, or it may be associated with the preliminary movement of the diaphragm.

Summary

Simultaneous cineradiography and pressure recordings were made in ten normal subjects during the passage of barium through the gastroœsophageal junction. In the first series of experiments the subjects were given barium to hold in the mouth and to swallow later when the œsophagus was at rest. Under these conditions the barium was held up at the gastroœsophageal junction, which slowly opened after a pause. The opening of the junction was accompaned by a fall in pressure in this area. These findings indicate a sphincteric mechanism at the gastro-œsophageal junction; it appears to be situated in the lowest 2 to 3 cm. of the œsophageal tube. The sphincter may be forced open prematurely by a sufficiently high intraœsophageal pressure.

In the second series of experiments the subjects were given the same volume of barium to drink off from a cup. Under these conditions the barium passed straight through the junction without delay and, further, the junction appeared widely open as the barium arrived. The act of drinking was preceded by a descent of the diaphragm. These observations indicate that drinking and swallowing are different physiological processes, and that the gastroœsophageal sphincter is opened earlier in drinking than in swallowing.

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PUERPERAL SURGERY AND UMBILICAL HERNIA*

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SEVERAL conditions which may be found during pregnancy can be dealt with efficiently during the puerperium, especially when the delivery has been in hospital. Advances in obstetrical treatment and the enormous reduction in the incidence of puerperal sepsis have made the puerperium an uneventful period of recovery for most women; and the time can be used for certain operations with advantage both to the hospital and the mother.

Advantages

Many arguments support a decision to operate during the puerperium. The patient must be at rest in any case for 10–14 days. Experience shows that tissue healing is unusually efficient at this time; extensive scarring found in gynæcological outpatients bears witness to previous injuries to the cervix, vagina, or perineum of which the patient knows little. Perhaps the relatively high levels of ovarian hormones persisting after delivery encourage healing. Involution reduces the dimensions of minor surgical errors to barely recognisable proportions. Many tissues, hypertrophied by pregnancy, are conveniently lax and have an extremely rich blood-supply. Dissection is unusually easy. For these reasons operation on urinary fistulæ has been recommended during pregnancy, especially when several previous operations have failed, leaving much avascular scar tissue.

Other and more positive indications for early puerperal surgery include an ovarian cyst which may have been damaged during labour, and intestinal complications for which prompt operation is imperative.

It is often a kindness to combine what would otherwise be two separate episodes in hospital, since arrangements have generally been made for care of the home and other children. Many mothers with young children neglect their own health until symptoms become intolerable, and by then treatment may be more hazardous and less successful. It is among obese multiparæ, to whom these remarks especially apply, that umbilical hernia is most commonly found.

Scope of Surgery

I have often been encouraged to do certain operations early in the puerperium and, though little has been

* Based on a paper read to the North of England Obstetrical and Gynæcological Society on March 15, 1957.

published about doing operations then, I am sure the practice is widespread. The modern policy of repairing fresh third-degree perineal lacerations in an operating-theatre, with good anæsthesia, lighting, and assistance, rather than in a labour ward, is so satisfactory that it has been extended to the planning of elective repair of various faults found during the antenatal period. For example, old-standing unhealed third-degree tears, and recto-vaginal fistulæ have been repaired within a few hours of delivery with excellent results, perhaps even better than in patients with similar lesions admitted from a gynæcological waiting-list. Laxity of the perineum and a rectocele can be similarly dealt with, but allowance must be made for the effects of involution and the vaginal introitus left much slacker than in the ordinary patient.

Umbilical hernia is not often considered in connection with pregnancy, but a tragedy some years ago suggests that this view might be revised.

A married woman, aged 42, para-9, was first seen in August, 1954, in labour at term, with an irreducible umbilical hernia as big as a saucer. An uneventful assisted breech delivery took place, and progress was normal for the next twenty-four hours. The possibility of a bowel accident within the hernia was constantly in mind—in fact this had been the reason for the patient's admission to hospital—so, when the patient began to complain of pain in the umbilical region the day after delivery, a surgical consultation was arranged. Conservative management was recommended, because, in the absence of vomiting, it was thought that the hernia contained omentum only; but the patient's condition deteriorated, and sixty-two hours after delivery laparotomy was done. Strangulated terminal ileum and omentum were found in the hernial sac. Ten inches of ileum was resected, but despite all resuscitative measures the mother died eleven hours later.

It is well known that the signs and symptoms of intestinal complications are much altered in the puerperium, largely because the abdominal wall is so flaccid after the uterus has emptied that it does not react as it does in the non-pregnant; hence, guarding and rigidity are often absent until the late stages. The patient may not vomit (Woodruff and Epperson 1952) and fluid levels should be sought by X-ray examination. Early laparotomy must be performed if doubt persists. Strangulation is especially difficult to diagnose in the fat woman with a small hernia; if the layer of fat is deep enough, gut may be trapped at the fascial neck without any visible swelling at the skin surface (Watson 1948).

The fatal case reported above shows that an umbilical hernia can become strangulated as a result of pregnancy or of labour, but such an event has rarely been recorded.

Pott (1756) cautioned against the disastrous results of rupture of the sac during pregnancy.

A strangulation at the twenty-second week of pregnancy was successfully treated by immediate repair (Newman 1947).

Boys (1945) recorded a case in which the pregnant uterus at term became strangulated in a large umbilical hernia and cæsarean section was necessary before the hernia could be reduced. Five largely similar cases previously reported are described in the same paper.

In some of these instances the hernia was successfully repaired after an emergency operation, but I have been unable to trace any suggestion that repair should be done in the immediate post-partum period as a prophylactic procedure.

Umbilical Hernia

Umbilical hernia is caused by increasing abdominal pressure, most often from repeated pregnancy and obesity. The adults affected are almost always in obese multiparæ at the end of the childbearing period (Aird 1949). The hernia is generally progressive and is liable to obstruct or to become strangulated. Operation for strangulation has a huge mortality, variously estimated at 30–50%, a much graver prognosis than for strangulated inguinal or femoral hernia (Watson 1948, Aird 1949). Even without strangulation, operative repair can be hazardous because the return of quantities of gut and omentum to the abdomen, for which the hernia has acted as a safety-valve, leads to increased pressure on the diaphragm and interference with venous return. Post-operative chest complications, cardiac failure, and recurrence of the hernia are common (Bartlett 1952). Drastic weight reduction is the only way in which the prospects for a successful operation can be improved in the worst of these cases. With a growing uterus to increase the strain, repair during pregnancy must be highly unsatisfactory.

The immediate postpartum period, therefore, seemed an ideal opportunity for formal repair, both to avoid the consequences of strangulation following labour and to take advantage of the sudden reduction in abdominal contents by delivery, when the abdominal wall will be slacker than at any other time in the patient's life.

Experience of Effective Repair

Weakening of the umbilical cicatrix is common in late pregnancy, and a defect admitting the finger-tip, with a small protrusion on coughing, is often seen. Since 1954 a larger deficiency amounting to true umbilical hernia has been observed in 17 patients attending the University obstetric units at the Jessop and City General Hospitals. Of these patients, 7 were obese multiparæ so busy bearing and rearing children that they would spare no time for themselves. Five of the hernias were large irregular masses, two of them being irreducible. Three of the smaller hernias were also irreducible.

Twelve of these hernias were repaired within forty-eight hours of delivery with complete success. Except one hernia treated by upward extension of a subumbilical incision on completion of cæsarean section, all were operated on by a standard Mayo technique:

The umbilicus is excised by a transverse elliptical incision cleansing about one inch of anterior rectus fascia above and below the defect. The hernia is opened at its neck, where adhesions are least likely to develop; gut is returned to the abdomen, and the peritoneal sac together with any adherent omentum is excised. After closure of the peritoneum the fascial flaps are overlapped transversely, catgut sutures being used. Superficial fat and skin are then closed without drainage.

Gross lesions were found, with extensive adhesions between bowel and omentum, and containing multilocular cavities in which the risk of strangulation must have been great. The operations were technically straightforward, and the wounds all healed by first intention. Good overlap, without tension, was possible even when large deficiencies were closed.

Three patients declined treatment; one, who had had, during pregnancy, intermittent pain suggesting subacute obstruction, suddenly changed her mind about repair after delivery and took her own discharge against advice. The risk of serious complications in the obese multipara is increased by such self-neglect; unfortunately this is the very type of person who most often does not seek advice when the need should be clear and ignores it when it is given. Another repair was postponed because obstetric complications required two anæsthetics before delivery; a third was judged unwise within so short a time. The hernia was reasonably small and could be left for a later occasion without great risk. The remaining case is undelivered.

8 patients operated on between nine months and two years ago have been re-examined recently, and no recurrences have been found. Recurrence is said to be commonest in the first six months after operation and it is rare after a year in the absence of severe strain, as an example of which Watson (1948) cites pregnancy. In my first case the patient became pregnant less than three months after operation and was delivered normally at term less than a year after puerperal repair of a particularly large defect. The repair remains intact.

Discussion

More than one patient remarked that her lesion had been noted during a previous pregnancy, but the obstetrician had advised that it should be attended to later. Later means never to many such women.

The puerperium can be used to great advantage for elective surgical treatment if plans are made in advance. It is a convenience to the patient to recover simultaneously from delivery and an operation, always provided that no complications would increase the risks of operation. The time of hospital staff and accommodation are often wasted because patients do not come for admission when sent for, particularly in the case of mothers of young families beset by domestic difficulty. Such waste, when waiting-lists are long and beds few, can sometimes be avoided by planning treatment during pregnancy; and this is especially true for the irresponsible patient whose lesion is a constant source of danger to her. For such people treatment which can be given while they are already under medical supervision has the great virtue that it *is* given.

Summary

Many abnormalities observed in pregnancy, though not likely to interfere with childbirth, can well be treated in the early days of the puerperium.

The anxiety of the patient to cooperate during pregnancy is an asset of great value in improving the health of the community.

Surgical repair of umbilical hernia is highly satisfactory when done within a few days of childbirth, when the abdomen is slacker than at any other time. The dangers of neglect are shown by the record of a fatal case in the puerperium, and the treatment of 17 cases of umbilical hernia in pregnancy is reviewed.

Other operations, such as the repair of old-standing third-degree perineal tears, fistulæ, and rectocele and the removal of ovarian cysts are recommended to be done while the patient is still in hospital after confinement.

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IRON METABOLISM DURING TREATMENT OF IDIOPATHIC HÆMOCHROMATOSIS

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THE excessive quantities of iron deposited in the body-tissues in idiopathic hæmochromatosis are believed to produce changes which determine the clinical features of the disease. The prognosis is variable: although some patients may survive for many years with minimal inconvenience, the average expectation of life is said (Finch and Finch 1955) to be about four and a half years after the onset of symptoms. It is impracticable to limit the intake of iron, to prevent its absorption, or to increase its excretion to a useful extent with chelating agents; however Finch et al. (1950) showed that iron stores could be effectively depleted by repeated venesection, and it has become accepted practice to treat hæmochromatosis in this way.

TABLE I—DETAILS OF PATIENTS TREATED BY VENESECTION

Case no.	Age at onset (yr.)	Age in 1957 (yr.)	Clinical features: Hepatomegaly	Pigmentation	Diabetes	Hypogonadism	Cardiac disease	Serum-iron level (μg. per 100 ml.)	T.I.B.C. (μg. per 100ml.)
1	36	43	+	+	+	+	−	295	
3	53	55	+	+	+	+	−	256	278
9	45	55	+	+	+	−	−	182	196
12	30	34	+	+	−	+	−	343	350
13	64	67	+	+	−	+	+	277	303
14	63	68	+	+	+	+	−	232	

Davis and Arrowsmith (1952) first described the results of this treatment, and McAllen et al. (1957) review their own experience and that of other workers. It is common to draw blood at the rate of about 500 ml. a week; this removes 250 mg. of iron from the body. Some workers, however, bleed their patients more severely. Hæmoglobin levels are well maintained by the utilisation of iron from stores which thus become progressively depleted. Treatment is accompanied by subjective and objective clinical improvement, and the diminution of the siderosis in the liver and elsewhere may be expected to arrest the progress of the disease.

In the untreated patient the serum-iron level is high, and the total iron-binding capacity of the serum (T.I.B.C.) is nearly saturated, except in the presence of infection. When all the available deposits of iron have been used up, the serum-iron level is low and the T.I.B.C. is increased. These changes take many weeks to develop, follow a clearly defined pattern, and regularly precede any definite decrease in the amount of hæmoglobin. Davey et al. (1954) observed that, in their patient, the serum-iron level fell before severe anæmia developed.

We show here how regular and frequent determinations of the serum-iron level and the T.I.B.C. can be used to predict the ultimate exhaustion of available iron stores and thus to forestall the development of anæmia.

Materials and Methods

15 male patients with idiopathic hæmochromatosis were studied, of whom 7 died before venesection was started. Of the remainder, 6 patients (cases 1, 3, 9, and 12–14) had frequent venesections during periods which ranged from six month to four years. In all the cases the diagnosis was established on clinical grounds and after

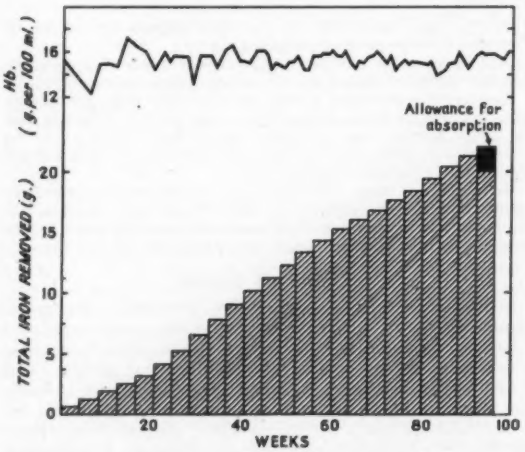

Fig. 1—Case 14: hæmoglobin levels during depletion of iron stores by venesection.

laboratory investigations. Particulars of the 6 patients are summarised in table I. All of them, at the time of diagnosis, had enlarged livers and pigmentation of the skin, and 4 were diabetic. In 5 patients the serum-iron level was high, whereas in the 6th it was just within the normal range (Ramsay 1957a). The T.I.B.C. was determined before the beginning of venesection in 4 of the patients, and in each case the iron-binding capacity was almost saturated.

Venesection was usually done weekly, but in cases 9 and 13 it was less regular. Case 9 was bled irregularly only because his work involved much travelling away from town, and case 13, who is subject to recurrent severe respiratory infections, was the only patient who did not tolerate regular bleeding satisfactorily. Usually about 550 ml. of blood was withdrawn each week. When massive venesection was discontinued, 20-ml. samples were

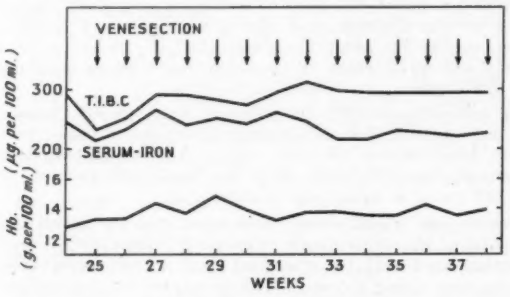

Fig. 2—Case 3: hæmoglobin, serum-iron, and T.I.B.C. during venesection.

taken for analysis. Determinations of serum-iron (Ramsay 1957a), T.I.B.C. (Ramsay 1957b), and total blood-iron (Ramsay and Campbell 1954) were made on all the samples, and hæmoglobin concentrations were calculated from the figures for total iron. The diet and insulin requirements of the 4 diabetic patients were supervised at each visit.

Results

During treatment by venesection the hæmoglobin concentration in the blood appeared to remain fairly stable for periods varying from nine to thirty months. Analyses, however, were not made between venesections; hence the values obtained do not show that, in the twenty-four hours following withdrawal of blood, the amount of hæmoglobin decreased but increased again in a few days as long as iron was available. In several cases the weekly hæmoglobin levels tended to rise above the basal value, but the usual pattern was of narrow fluctuation about a mean level which was characteristic of the patient. This is illustrated in fig. 1, which shows the hæmoglobin determinations in case 14 over two years, during which about 20 g. of iron was removed by venesection.

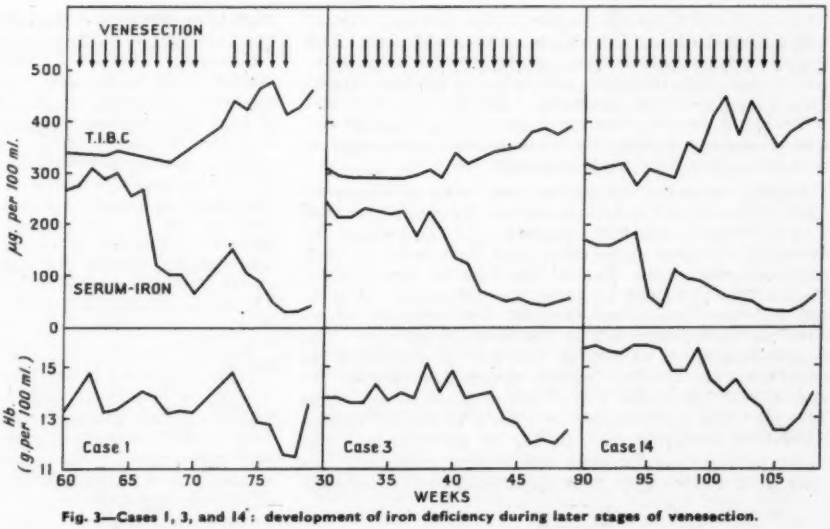

Fig. 3—Cases 1, 3, and 14: development of iron deficiency during later stages of venesection.

Early in the initial period of venesection the serum-iron level and the T.I.B.C. usually remained near their original values, but in some patients the serum-iron level later tended to fall gradually. This phase is illustrated for case 3 in fig. 2. A transient precipitate fall in the serum-iron level was occasionally observed. Sometimes these episodes could not be explained, but in cases 13 and 14 they were related to the respiratory infections to which these patients were liable.

In each of the 5 patients in whom a state of incipient anæmia was produced, however, a steep and lasting fall in serum-iron level to subnormal values preceded by from four to eight weeks any persistent decrease in hæmoglobin. At the same time the T.I.B.C. increased; thus, by the time the hæmoglobin level reached 12 g. per 100 ml., the T.I.B.C. might be 100 μg. per 100 ml. above its original value. The development of this pattern, which resembles that seen in the anæmia of iron deficiency, is illustrated for cases 1, 3, and 14 in fig. 3.

At this stage, when the hæmoglobin had decreased to 11–12 g. per 100 ml., regular massive venesection was stopped. In each case the fall in serum-iron level was arrested, as can be seen in fig. 3. The hæmoglobin reverted to normal in a period varying from two weeks to three months, but usually the serum-iron level returned

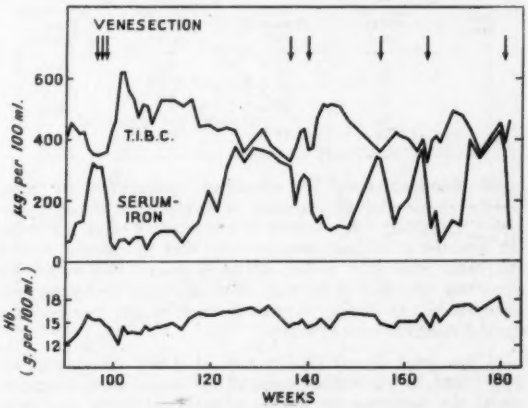

Fig. 4.—Case 12: hæmoglobin, serum-iron, and T.I.B.C. during maintenance treatment.

very much more slowly to the value characteristic of hæmochromatosis. The T.I.B.C. remained high, and might even continue to rise for some weeks after venesection had been stopped, and after the fall in serum-iron level had been arrested. Ultimately, however, the original pattern was again seen, with high serum-iron levels, and a high saturation of the T.I.B.C., and at that stage venesection was resumed.

Usually a single venesection was then sufficient to cause a return to the low serum-iron level and the high T.I.B.C., which together suggest the imminence of anæmia. Unless venesection was continued in such circumstances, there was no decrease of hæmoglobin. Venesection sufficient to cause the serum-iron level to fall and the T.I.B.C. to increase was repeated whenever the values returned to the original pattern. The management of a patient in this way is illustrated for case 12 in fig. 4. This patient apparently requires the removal of about 500 ml. of blood about every three months. The maintenance of case 1 in similar fashion involves venesection once in five or six months. The other patients require even less frequent bleeding now that their initial stores have apparently been exhausted.

Discussion

Serial weekly determinations of the serum-iron level, the T.I.B.C., and the hæmoglobin provide data on which to base the treatment of each patient. Occasional and random estimations are of little value; even the monthly observations advised by Finch and Finch (1955) are inadequate for satisfactory control. In the present cases it would have been possible to dispense with the measurements of the T.I.B.C., but it is obvious from figs. 3 and 4 that they make the pattern of incipient deficiency of iron much more clear.

The frequency with which venesection is required during maintenance therapy must bear some relationship to the capacity of the patient to absorb iron. In our limited experience more frequent venesection has been necessary in those younger patients from whom larger quantities of iron have been removed during the initial depletion of iron stores. In table II the ratio of the quantity of iron thus removed to the age of the patient at the onset of symptoms is compared with the time that elapsed until further bleeding was indicated ("reversion time"). This "iron/age ratio" is a rough index of the patient's ability to absorb iron during the development of hæmochromatosis. Comparatively

TABLE II—RATE OF ACCUMULATION OF IRON

Case no.	Age at onset (yr.)	Iron removed (g.)	Iron/age ratio (g./yr.)	"Reversion-time" (mos.)
1	36	17·2	0·5	5–7
3	53	11·4	0·2	17
9	45	10·4	0·2	>8
12	30	21·5	0·7	3–4
13	64	Iron stores not exhausted		
14	63	26·8	0·4	>16

rapid accumulation of excessive quantities of iron should cause the appearance of symptoms at an early age. The "iron/age ratios" for cases 1 and 12 were 0·7 and 0·5 g. a year respectively, but in cases 3 and 9 the ratio was only about 0·2 g. a year. As would be expected, the first pair, who were also the two youngest patients in the series, require more frequent venesection during maintenance therapy.

It has been found (Balfour et al. 1942, Chodos et al. 1957) that, in established cases of idiopathic hæmochromatosis, the patients no longer absorb excessive amounts of iron, unless the iron stores have been depleted by venesection (Chodos et al. 1957). Other workers (Dubach et al. 1948, Bothwell et al. 1953) have reported abnormally high absorption of iron in patients who had not been venesected. There were wide variations in the experimental conditions used by the different groups of workers. Although we did not measure the absorption of iron, the relationship between the "iron/age ratio" and the frequency with which venesection must be repeated during maintenance therapy (table II) suggests that in our patients venesection did not greatly alter the rate of absorption previously characteristic of each patient. Bothwell et al. (1953) found that their only 2 young patients absorbed very large proportions of orally administered radioactive iron. This is in keeping with our observation that our 2 youngest patients (cases 1 and 12) had accumulated more iron relative to their age than had the other patients.

Careful attention to the information derived from frequent analyses of samples of blood makes it possible to control treatment and to avoid the development of anæmia in the uncomplicated case of hæmochromatosis. Occasionally, however, other factors, such as infection and coincidental disease, may (as in case 13) make the data obtained of less value and more difficult to interpret. It should, moreover, always be remembered that patients treated in this way may not possess even normal iron reserves and are therefore more liable to become anæmic if hæmorrhage takes place because of trauma or of illness.

Summary

Weekly determinations of serum-iron levels and of the total iron-binding capacity of the serum in 6 patients with idiopathic hæmochromatosis undergoing regular massive venesection showed that the development of anæmia was always preceded by a large fall in the serum-iron level and an increase in the total iron-binding capacity of the serum.

Venesection should be stopped when these changes take place and should be resumed only when the serum-iron level returns to the high values associated with hæmochromatosis and when the iron-binding capacity of the serum is again almost saturated.

After the initial series of venesections, by which the available iron stores are exhausted, subsequent venesection need only be infrequent, and seldom more often than four times a year. The frequency of subsequent venesection is apparently related to the capacity of the patient to absorb excess quantities of iron. This may be roughly predicted from the age at which symptoms become apparent and the quantity of iron removed during the initial period of venesection.

We wish to thank Dr. J. B. Tucker, Dr. W. J. H. Leckie, and Dr. G. D. Campbell for their successive assistance in the care of these patients; Miss Winifred J. Martin for her technical help; and Prof. D. M. Dunlop for his interest in this work.

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ORAL DEPOT THERAPY WITH A NEW LONG-ACTING DEXAMPHETAMINE SALT

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IT will be generally agreed that a therapeutic ideal is the oral administration of a single dose of a drug in such a form as to ensure its sustained continuous absorption over an extended period of time, maintaining a uniform optimal level in the tissues; so avoiding, on the one hand, unnecessarily high peak concentrations and, on the other, wasteful depressions. The manifold advantages of what may aptly be termed oral depot therapy demand no emphasis in recommendation; they include certainty of continuity, no relapse due to forgotten doses, and convenience.

To secure prolonged action, it has been the usual practice to release a drug at intervals by presenting it in a mixture of variously treated granules or enteric-coated 'layered' tablets. Since, however, disintegration depends on individual physiological factors (peristalsis, pH, &c.), regular absorption by these means cannot be assured.

In contrast to these physical methods, sustained action can be satisfactorily achieved by a reliable chemical process.

Chaudhry and Saunders (1956) have shown that the chemical combination of a drug with an appropriate ion-exchange resin produces a drug-resin salt which, when acted on by the ions in the digestive juices of the gastrointestinal tract, will liberate the drug for absorption evenly over an extended period of time. Basic drugs combine with an acidic ion-exchange resin to yield a "resinate," and acidic substances combine with a basic resin to yield a resin-salt.

The reactions involved may be summarised as follows:

Formulation

(1) Acidic ion-exchange resin + basic drug $\rightleftharpoons$ drug resinate.
(2) Basic ion-exchange resin + acidic drug $\rightleftharpoons$ resin salt.

Liberation

In the stomach:

(1) Drug resinate + HCl $\rightleftharpoons$ acidic resin + drug hydrochloride.
(2) Resin salt + HCl $\rightleftharpoons$ resin chloride + acidic drug.

In the intestine:

(1) Drug resinate + NaCl $\rightleftharpoons$ sodium resinate + drug hydrochloride.
(2) Resin salt + NaCl $\rightleftharpoons$ resin chloride + sodium salt of drug.

Both the drug resinate and the resin salt are completely insoluble. The release of the active principle (shown in equations 1 and 2) is controlled by the normal laws governing velocity of chemical reactions and is unaffected by enzyme action, peristalsis, or other physiological processes.

Dexamphetamine Resinate

'Dexten' is a dexamphetamine-resinate tablet with such properties. The release of dexamphetamine in dexten depends solely on the availability of ions; and, since the total concentration of these in the gastrointestinal fluids is within narrow limits constant, the rate of interchange between the resinate and the ions, and thus the rate of release and subsequent absorption, are also constant. Dexten has thus been designed to provide a depot from which dexamphetamine is released evenly and at a constant level over an extended period and thus to avoid the undesirable fluctuations of concentration in the tissue fluids which are bound to result from intermittent dosages with unbonded dexamphetamine. Losses due to normal metabolic processes and to excretion are being constantly restored, with the result that a smooth uninterrupted therapeutic effect is obtained lasting 10–12 hours. An additional advantage is the considerable reduction of the danger of acute poisoning (Newbold 1957, Margulies 1957).

The rate of release of dexamphetamine from dexten, determined by in-vitro experiments is as follows:

Time after Ingestion (hrs.)	*Amount Liberated (%)*
2	26
4	41
6	51
8	62
10	75
12	85
14	85

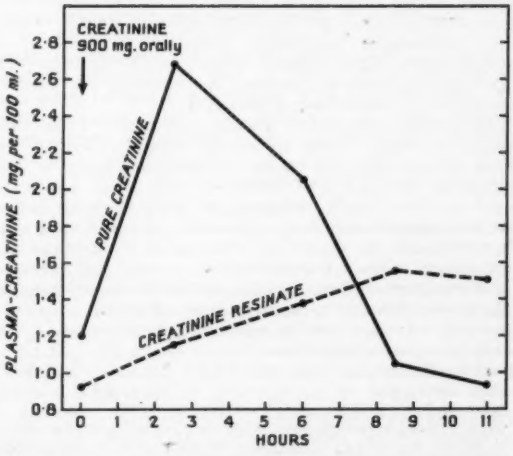
Concentrations of acidic and alkaline ions corresponding to those found in the stomach and in the intestine respectively have been utilised in succession for the dissociation. It will be seen that equilibrium is reached after 12 hours when about 85% of the dexamphetamine has been liberated from the resinate, at which stage exactly the same amount of drug combines with and is released from the resin. Hence the residue remaining in the resin is not released and no accumulation occurs. This has been proved both in vitro and pharmacologically.

The in-vitro results have been confirmed by experiments on rats, the convulsant effect of dexamphetamine being used as the significant end-point. It has been established that the resin used to form the resinate is completely inert and therefore free from danger, even when massive doses are used, as in the treatment of gastric disorders.

In-vivo Tests

The rate of absorption of drugs from drug resinates has been confirmed in vivo by Prof. A. Kekwick (1957) using creatinine as a marker. Creatinine was chosen as a suitable experimental substance because its behaviour in the body is well understood; large doses of it can be given without ill effect, and methods of assaying it are reliable. It is possible to measure accurately the creatinine content of the blood and urine, a procedure inapplicable to most therapeutic substances, including amphetamine.

The accompanying figure shows that in 5 people, after the oral administration of 900 mg. of pure creatinine, the blood-creatinine level reached a peak in two hours, falling steeply thereafter to normal in about eight hours. When the same amount of creatinine was given as a resinate, absorption was delayed, and a high blood-



Absorption of creatinine 900 mg. given orally alone and as creatinine resinate. Each graph shows mean of 5 persons.

creatinine level was sustained over a much longer period, high levels being still in evidence long after ten hours.

The in-vitro release patterns of most drug resinates—e.g., ephedrine, dexamphetamine, hyoscine, and amylobarbitone—and creatinine are very similar. Since the in-vitro and in-vivo results with creatinine resinate correspond, it may reasonably be assumed that the position is the same with other drug resinates.

Clinical Observations

Amphetamine has been described as a versatile drug used in, and proved of value for, many diseases and disorders (*Lancet* 1947). It is considered here only as an adjuvant in the treatment of obesity. As is well recognised amphetamine does not directly get rid of weight; it reduces appetite or hunger partly by inhibiting contractions of the stomach, partly by direct action on the cerebral cortex. It removes the mental depression and physical lethargy consequent on a diet of low calorie value, it shields the patient against the inevitable discomfort, and to some extent it enables him to acquire and retain new dietetic habits.

Clinical trial was applied in practice by several general practitioners, for periods of two to sixteen weeks, to 53 ambulatory obese patients. The trials were coordinated, and the result of the critical examination of the 53 case-reports may be summarised as follows:

7 men and 46 women, aged 23–58, were given the ordinary dexamphetamine therapy for various periods before being given dexamphetamine resinate. Each patient was given at breakfast a single tablet of dexten containing dexamphetamine sulphate 10 mg. as resinate or of 'Barbidex' containing dexamphetamine sulphate 10 mg. as resinate plus phenobarbitone 65 mg. (gr. 1).

Weight-loss was variable, as is only to be expected, partly because of various individual constitutional factors, partly in proportion to the degree of strictness with which the dietetic regime was practised. The average loss was 6 lb. in four weeks. One patient lost 7 lb. in the first week, and another 14 lb. in four weeks.

Discussion

As was anticipated from the comparison of in-vivo and in-vitro tests with creatinine, the average duration of effect appeared to be longer than indicated by the in-vitro tests. The release of dexamphetamine in vivo (as in vitro) ceases on equilibrium being reached after about eight hours, but the therapeutic effect of the dexamphetamine released during the eighth hour continues for about 4 more hours, this being the normal average duration of activity of dexamphetamine given alone. About 85% of the patients achieved satisfactory control of appetite for twelve to fourteen hours; about 3% experienced insomnia, indicating a duration of action longer than fourteen hours. Such patients were promptly relieved of insomnia by reducing the dose of dexten or by substituting barbidex.

Subjective sensations usually referred to the chief point at issue—power to refrain from "nibbling" or from snacks between meals. During treatment a mild elevation of mood was noted in most cases, but in no case did this reach a level which impaired judgment or routine daily activities. A sense of well-being and improvement in ability to concentrate were frequently mentioned. The resinate enabled the anorexic property of dexamphetamine to be made available to patients who could not tolerate ordinary dexamphetamine. Many patients remarked on the convenience of having to take only one dose at breakfast.

Side-effects were few and mild. Dizziness and headache developed so infrequently as to suggest strongly that the patients were relatively more tolerant of dexamphetamine resinate than of pure dexamphetamine. Euphoria in a few instances amounted to excitability, but was soon overcome by substituting barbidex for dexten.

In only 2 cases was it necessary to discontinue the treatment because of an unusual degree of intolerance to amphetamine. An uncommon side-effect of amphetamine—i.e., dryness of the mouth, complained of by 1 patient—was abolished by reducing the dosage from 1 to ½ tablet.

Summary

The principle of providing prolonged continuous even absorption by a single dose of orally active drugs in general and of dexamphetamine in particular from compounds with ion-exchange resins is described.

The advantages of oral depot therapy with drug resinates over existing physical methods of delaying disintegration are outlined.

In-vivo experiments with creatinine resinate support observations in vitro, with results that may be applied to the administration of amphetamine and other drugs.

Clinical trials with 'Dexten' (dexamphetamine resinate) and 'Barbidex' (dexamphetamine resinate plus phenobarbitone) in obesity are described. The average duration of inhibition of appetite after ingestion of 1 dexten tablet or 1 barbidex tablet was twelve hours, and the average loss of weight of 53 patients was 6 lb. in four weeks.

Side-effects were both fewer and less severe than those experienced by the same patients given even smaller doses of unbonded dexamphetamine; patients sensitive to dexamphetamine tolerated it as the resinate.

We are indebted to Clinical Products Ltd., of Richmond, Surrey, for the 'Dexten' and 'Barbidex' ('Ionexten' brand) sustained-action tablets used in the clinical trials.

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THE PROGNOSIS OF URINARY INFECTIONS IN CHILDHOOD

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SEVERAL reports suggest that urinary infections in infancy and childhood may have less favourable outcomes than is usually supposed:

Kromann (1950) treated 15 children by "rational chemotherapy" (based on sensitivities of the infecting organisms) and reported 5 failures; Anderson and Lund (1954) had 4 failures among 33 children treated with various antibiotics; and Stansfeld (1954) states that 60% of urinary infections in early childhood are or become chronic.

The best follow-up we know of is that of Woodruff and Everett (1954), who recalled 76 females who had had pyuria in childhood, from five to twenty-three years before, and investigated their urinary tracts: 49% had had one attack only and no evidence of renal disease on re-examination; 22% had had only one clinical episode, but had some abnormality of the renal tract at follow-up; and 29% had had repeated attacks of urinary infection.

More general statements are made by Taylor (1955), according to whom pyelonephritis "is a recurrent disease which can persist even after all clinical and urinary signs have cleared"; and by Beeson (1955): "It is generally believed that the pyelonephritis of infants has the same potentialities for chronicity and serious complications as other forms of the disease."

In view of the seriousness of these statements and the relative paucity of information on this subject we tried

to determine the fate of the infants and children with pyuria treated at this hospital in 1950 and 1951.

Material

In 1950 and 1951 32 children were admitted with urinary infections. In all of them the centrifuged deposits of fresh specimens of urine contained more pus cells than are usually found. All these examinations were made by one technician, who examined nearly two thousand specimens of urine in those two years. The same technician examined the specimens of urine in the follow-up study. In all 32 children cultures of catheter specimens of urine were positive. We have omitted a considerable number of cases with mild pyuria and negative cultures; many of these were in children with acute febrile illnesses in whom the pyuria was probably of little significance. In the 32 remaining cases a urinary infection was accepted as the cause of the symptoms or an important part of the disease.

The incidence of urinary infection was 1·1% of 3066 admissions, which is similar to the experience of others (Stansfeld 1954, Engel 1955).

The ages of the patients at the time of admission ranged from 3 weeks to 4½ years; 12 were aged less than 1 year. There were 22 girls and 10 boys; this sex ratio is in accordance with the common experience that acute renal infection is a disease mostly of girls. 30 patients received chemotherapy, of which the details are omitted because many different drugs were used either alone or in combination, and the numbers were too small to yield useful information.

Follow-up

Of the 32 patients 5 were untraced; 1 of these had left the country; but we got some information about the subsequent health of the 4 others. The 27 who were traced comprised 6 boys and 21 girls.

5 boys with gross abnormalities of the genito-urinary tract had died: 2 of them died of renal failure; 2 from overwhelming infections (*Escherichia coli* septicæmia in one and staphylococcal pneumonia in the other); and 1 from cerebral hæmorrhage. The 5 renal anomalies were posterior urethral valves with pyonephrosis and hydronephrosis in 2 cases; a recto-urethral fistula which broke down repeatedly after attempted repair in 1 case; bilateral mega-ureter and hydronephrosis of uncertain ætiology in 1 case; and an atrophic kidney with contralateral pyonephrosis in 1 case.

Of the 22 surviving children, 16 were re-examined, and information about the health of the 6 others was obtained by submitting a detailed questionnaire to their parents and their local medical attendants.

Of the 16 patients examined only 8 had had no subsequent history of urinary infection, were physically normal on examination, and had normal urine:

3 children were chronically ill with urinary infections: 1 had had a bladder-neck resection for relief of bilateral mega-ureter and trabeculation of the bladder; 1 was diagnosed as having neurogenic dysfunction of the bladder and had complete urinary incontinence; and 1, although numerous investigations of the renal tract had not revealed any organic abnormality, had persistent pyuria, with recurrent episodes of acute infection, during the five years before the follow-up examination.

2 girls had had single further episodes of pyuria after the initial one but were well and had normal urine on re-examination.

1 girl had had repeated urinary infections but on re-examination was healthy and had normal urine; extensive urological examinations had not revealed any anatomical lesion underlying these infections.

2 children were physically normal on examination and had no history of subsequent urinary infections but their urine contained a small but significant number of pus cells at follow-up. One of these children had undergone partial nephrectomy and removal of an ectopic ureter on the initial admission.

RESULTS OF FOLLOW-UP

	No. of patients	Total
Re-examined:		
No abnormality	8	
Well; mild pyuria	2	
Recurrent infections; well on re-examination	3	
Chronic renal disease	3	16
Questionnaire information:		
Well	5	
Chronic renal disease	1	6
Deaths		5
Untraced:		
Subsequent health unknown	1	
Further renal disease known	3	
Mild pyuria 1½ yr. later	1	5
Total		32

5 of the 6 children who were not re-examined but concerning whom satisfactory replies were received were reported to be quite healthy. The other 1 was stated by her doctor to have constant urinary trouble (nature unspecified) and to be a miserable undernourished girl.

The hospital records revealed further facts about 4 of the 5 untraced children:

1 boy was treated for a recurrent urinary infection at a later date; 1 other boy had been admitted to another hospital with pyuria and was there found to have a non-functioning left kidney on pyelography; 1 other boy was subsequently found to have hydronephrosis due to a ureteric stricture and was operated on; and 1 girl was readmitted a year and a half later with a respiratory infection and found to have mild pyuria.

Thus in only 1 case is there no information about the progress after the original infection.

These results are summarised in the accompanying table.

Discussion

We do not wish to generalise too widely from these figures, but it is possible to make some relevant observations in spite of the small numbers.

A urinary infection in a boy should give rise to suspicion that there is a renal anomaly present, and we agree with Anderson and Lund (1954) that in these circumstances excretion urography is indicated. 7 of the 10 boys in this series had congenital deformities of the urinary tract.

Chronic or recurrent urinary infections are often associated with such deformities, but in 2 of our cases no anatomical lesions were found. This sort of patient would probably benefit from long-continued chemotherapy as advocated by Stansfeld and Webb (1954), Weyrauch and Rosenberg (1954), and Engel (1955).

Pyuria in infancy and childhood is *not* a simple and easily controlled condition. In this small series less than half the patients who had an attack six or seven years ago have remained completely well subsequently. We agree entirely with the opinions of other workers cited above about the sinister potentialities of such pyuria.

Summary

The condition of 32 patients who had a urinary infection in infancy or early childhood was determined six or seven years later.

5 of them had died and were found to have gross organic deformities of the renal tract; 1 was untraced; 13 were apparently normal; and 13 had either recurrent or persistent signs of urinary infection.

Urinary infections in children should be regarded as potentially serious, and prolonged supervision of such cases is advocated.

We are grateful to the physicians and surgeons who permitted use of their case-records; and to the Friends of the Hospital, who made a grant to cover secretarial and other expenses.

references overleaf

PARADOXICAL ELECTROCARDIOGRAM IN CORONARY EXERCISE TEST

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THE term " angina of effort " is used to describe a pain due to coronary insufficiency and occurring as a result of exercise or emotion. In any given patient the pain follows the same pattern: it is usually first felt across the sternum and may radiate to one or both arms, to the jaw, or to the back. The characteristic of the pain is not its position but the fact that it is induced by exercise and, when such exercise is stopped, quickly subsides. It rarely lasts more than a few minutes. Emotion may also produce it. The pain is more easily brought on by exercise after a meal or in the cold or on a windy day.

Its relationship to coronary disease was first noticed by Heberden, and the following interesting characteristic of it has been known since those times: in certain individuals, after one or two stops due to the onset of pain, further exercise may produce no pain—patients seem, as it were, to have walked the pain off. One such patient seen by me was apt to suffer from typical angina of effort for the first game or so of tennis, after which he was free from the discomfort for the rest of his period of play, which might extend to several sets.

Master et al. (1944) correlated the electrocardiographic changes with a deficiency of oxygen in the inspired air. They found that the breathing of 10% oxygen would cause abnormalities in the electrocardiogram similar to those induced by their standardised exercise test. It is generally conceded that the pain is due to anoxæmia in a portion of the ventricular muscle, the site of origin of course varying from patient to patient. Since muscular catabolites are known to act as vasodilators, it is reasonable to suppose that when a patient with angina of effort

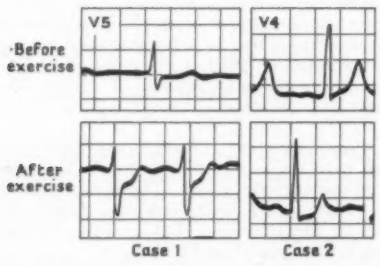

Fig. 1—Usual response to exercise test: in each case curve shows normal upright T wave with no significant depression of S-T segment. After exercise S-T segment is depressed, and T wave becomes in both cases diphasic.

walks off his pain he has succeeded in producing, as a result of the myocardial ischæmia, substances which cause vasodilatation in the local arteries and arterioles, thus removing the anoxæmia.

Master et al. were the first to use standardised exercises to elicit electrocardiographic deviations from the normal in patients with coronary disease. These deviations (fig. 1) were depression of the S-T segment, inversion of an upright T wave, and reversion to the upright position of an inverted T wave; but these workers do not specify, as regards the last-named finding, whether the change was a return to normal or the reverse.

Exercise tests are now commonly used to bring out latent electrocardiographic evidence of coronary disease when the resting tracing is normal in all leads. They are especially useful, when negative, in drawing attention to the presence of such conditions as gallstones and œsophageal abnormalities of function or of structure, which may, in rare cases, be responsible for chest pain simulating that of angina of effort and that of myocardial infarction. They must, of course, be used with discretion because fatalities have been reported.

The case here described is that of a man with angina of effort in whom the exercise test caused a reversed or paradoxical change in the electrocardiogram: a minor

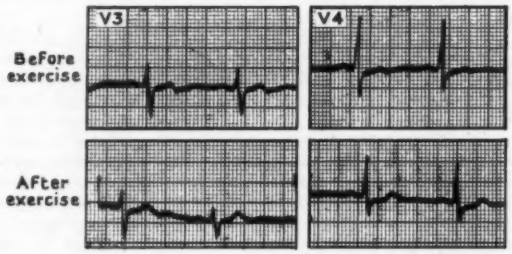

Fig. 2—Paradoxical response: before exercise in leads V3 and V4 T wave is diphasic, showing late inversion, and there is slight depression of S-T segment in V4. After exercise T wave becomes definitely upright in both leads, inversion having disappeared. The S-T segment remains depressed in V4. Thus effect of exercise is return towards normal—i.e., reverse of usual response.

but definite abnormality due to myocardial anoxæmia reverting, as a result of exercise, to normal. It is reasonable to suppose that such a phenomenon is the electrocardiographic equivalent of the above-mentioned clinical characteristic of walking off the pain which has been recognised for so many years.

Case-report

A man, aged 66, had two months' history of pain, which was localised chiefly in his left fore-arm but radiated thence to an interscapular area and thence to the upper substernal region. The pain would come on after he had walked about a quarter of a mile, but it would disappear after a few minutes if he rested. If he walked slowly he would not have the pain. It was associated with dyspnœa and occurred as a result of emotion. Ten days before his examination by me the pain once or twice became considerably more intense and caused him to feel ill. At these times he looked grey and was rather collapsed.

Physical examination was negative, except that his diastolic blood-pressure was slightly raised (blood-pressure 166/108 mm. Hg). Radiologically the heart was of normal shape and size, the transverse diameter being 13·0 cm. by orthodiagraph. The electrocardiogram (fig. 2) was normal in the standard leads, in the unipolar limb leads, and in leads V1, V2, V5, and V6. In leads V3 and V4, however, there was late inversion of the T wave characteristic of anoxæmia of the anterior ventricular muscle. Since the electrocardiographic abnormality was minimal, an exercise test was done in the hope of producing a more convincing result. This caused dyspnœa and tachycardia but no anginal pain. The two-step exercise entailed walking up and down two 9-in. steps fairly rapidly backwards and forwards thirty times. After reapplication of the electrodes the heart-rate had returned to its previous resting level, but the inversion of the T wave had completely disappeared.

I have been unable to find any published report of this paradoxical, but logically understandable, result of an exercise test.

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PSITTACOSIS WITH RELAPSE FOLLOWING AUREOMYCIN THERAPY

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PSITTACOSIS is endemic in the native psittacine and some other birds in Australia (Burnet 1934, 1935, Beech and Miles 1953, Surrey Dane and Beech 1955). The work of French et al. (1954) in Melbourne and Dorman et al. (1954) in Sydney has indicated that notifications of cases of this disease in man in Australia are proportional to the local provision for isolation and serological diagnosis of the virus.

Patients with psittacosis nowadays are usually treated with one of the tetracycline drugs—in most cases with a dramatic clinical response. We report here a case in which aureomycin (chlortetracycline) was given. Subsequently mild symptoms recurred; virus was still present in his sputum. A second course of treatment rendered his sputum free of psittacosis virus, and clinically he has remained well for nine months.

Case-record

An abattoir supervisor, aged 37, had malaise, headache, muscular pains, and high fever. On the third day his temperature was 103°F, and he had tachycardia and rapid respirations; heart-sounds normal; liver and spleen enlarged to palpation. The lungs were clinically clear, but a radiograph showed consolidation in the right mid-zone "suggestive of virus pneumonitis". Hæmoglobin 13·6 g. per 100 ml., leucocytes 7000 per c.mm. with normal differential count; erythrocyte-sedimentation rate (E.S.R.) 50 mm. in the 1st hour. Agglutinations for *Salmonella typhi*, *S. paratyphi*, and *Brucella abortus* negative. Paul-Bunnell test negative. Culture of urine and sputum revealed no pathogens. Repeated blood-cultures, including those for *Br. abortus*, were negative.

The fever continued, psittacosis was diagnosed clinically as the patient admitted recent close contact with budgerigars, and he had had a small epistaxis. Q fever was also considered because of his occupation. Beginning on the fifth day of the illness, aureomycin 250 mg. was given orally every six hours for twelve days. Fever subsided rapidly, and the spleen became impalpable and the chest radiographically clear. He appeared cured. Complement-fixation tests on the fourth day of this illness and fourteen days later were negative for Q fever, but positive for psittacosis (1 : 5 in the first specimen and 1 : 160 in the second).

Three weeks later the patient relapsed with fever and malaise for a week. There was no headache, but a cough with small hæmoptyses had developed. His temperature was 99·5°F, his spleen was again palpable, and there were clinical signs of pneumonitis at the right base with radiographic findings as before. Full blood examination was normal; E.S.R. 80 mm. in the first hour; agglutination tests again negative. A sample of sputum was collected for animal inoculation.

A second course of aureomycin, 250 mg. six-hourly, was given for eight days, again with rapid improvement. The patient's serum then gave a titre of 1 : 1280 in the psittacosis complement-fixation test. When last seen nine months after relapse he had remained well.

Isolation of Virus from Sputum

Isolation of the virus was not attempted when the patient was first admitted to the ward. After his relapse with return of pneumonitis despite the twelve-day course of antibiotic therapy, it was decided to attempt isolation of the virus from his sputum. A slightly bloodstained specimen of sputum was inoculated intraperitoneally into four-week-old mice. After eleven days they had a peritoneal exudate and an enlarged spleen. Passage of this mouse material to further mice or 7-day-old chick embryos resulted in the death of the chick embryos in a week and of the mice in two weeks. Smears of the peritoneal exudate from the mice or yolk-sac of the chick embryos which died of the infection showed elementary bodies which morphologically and tinctorially were typical of psittacosis virus.

Samples of the patient's serum obtained during his illness and a sample obtained three weeks after completion of his second course of treatment failed to show any evidence of recent infection with influenza A or B viruses.

Discussion

The clinical features and course of this man's illness, the rising titre of complement-fixing antibody to psittacosis virus, and the initial response to aureomycin therapy leave little doubt that he had an attack of psittacosis-virus pneumonia.

The carrier state after infection with this virus is the rule in the natural disease in birds. Myer and Eddie (1933), Bedson (1938), and Hurst et al. (1950) have shown that latent infection persists for a year or more in mice that have recovered from an experimental infection with psittacosis virus. There are, however, few recorded instances of the carrier state in man. Myer and Eddie (1951) have described a patient who was shown to be a carrier, excreting psittacosis virus in his sputum over at least ten years. In naturally infected parrots and pigeons, they have found that vigorous treatment with aureomycin rids these birds of virus (Myer and Eddie 1955).

From what is known about the pathogenesis of psittacosis infection in animals and the action of antibiotic drugs on the virus, the clinical improvement in the present case without elimination of the virus from the tissues is not unexpected. It is notoriously difficult to demonstrate neutralising antibodies, either in convalescent patients or in experimentally infected animals (Rudd and Burnet 1941). There is no doubt that in animals recovery is often associated with persistence of infection, and we must assume that, though immune mechanisms are functioning, they are relatively ineffective in eliminating all infective units. The tetracycline drugs prevent multiplication of the virus, and after treatment with one of them pronounced clinical improvement can be expected. If, however, on cessation of treatment viable virus is still present in the tissues, the degree of immunity may be inadequate to prevent multiplication of this virus, resulting in either clinical relapse or establishment of the carrier state.

In our patient the clinical relapse was relatively mild, but the virus was readily obtained from his sputum. It would be interesting, in a series of psittacosis patients, to test over a period of some weeks for the presence of virus following treatment with tetracycline compounds. Clinically most of these patients require fairly long convalescence from their infection, and this may be related to the interval between suppression of the virus by the antibiotic used in treatment and subsequent removal of the virus from the tissues.

Smadel et al. (1950), investigating the chemotherapy of scrub-typhus, observed clinical relapses after cessation of treatment in patients treated early in the disease. These workers assumed that these recurrences were due, at least partly, to failure to develop an adequate immune response. If this holds also in psittacosis, it might be desirable, after initial control of symptoms by an antibiotic, to allow a period of a week or more without treatment before giving the remainder of the course of the antibiotic.

Summary

Psittacosis pneumonia in a man aged 39 was confirmed serologically. After a twelve-day course of treatment with aureomycin 1 g. daily he had a relapse, and psittacosis virus was isolated from his sputum. He responded to a second course, with disappearance of virus from his sputum.

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† Drug Houses of Australia fellow to the clinical research unit of the Royal Melbourne Hospital and Walter and Eliza Hall Institute.

We wish to thank Sir Macfarlane Burnet of this institute for his interest and criticism, and Dr. Peter Warner of the Institute of Medical and Veterinary Science, Adelaide, for the complement-fixation tests.

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Reviews of Books

Mental Deficiency

L. T. HILLIARD, M.B., D.P.M., consultant psychiatrist and physician-superintendent, Fountain Hospital, London; BRIAN H. KIRMAN, M.D., D.P.M., consultant psychiatrist, Fountain Hospital, London; with the assistance of four contributors. London: J. & A. Churchill. 1957. Pp. 517. 60*s*.

EVEN today mental deficiency is often a neglected subject, and a new textbook is an event. When one of its "main themes is that mental defect is a wide social problem rather than a separate branch of clinical medicine," as Dr. Kirman claims, it deserves a special welcome and attentive reading.

It has in fact six contributors. Dr. Hilliard, who has acted as editor, is to be congratulated on the general arrangement and form of the book; it is logical, easy to read, and clearly set out. He has also contributed two excellent chapters on legal and administrative arrangements. We should have welcomed more from him; for instance, details on the joint use of staff with local authorities (which he rightly advocates) and other plans for the future.

The bulk of the book is by Dr. Kirman, who has provided practically all the central clinical section, with chapters which will be most useful to pædiatricians and general practitioners. He deals much more with the child than with the adult, but from the Fountain Hospital this is natural enough. Dr. Kirman has also written two short chapters on home care and advice to parents, which will be helpful guides to practitioners advising parents, especially those who prefer or who are forced to keep these children at home.

In two chapters, Dr. L. Crome has ably described the pathological changes in several varieties of mental defect, with a collection of excellent photographs. He has collaborated with Dr. Kirman in the chapter on causation; the result, however, is rather disappointing, perhaps because the subject is oversimplified, though there is an enormous list of references. Dr. Kirman (and later Dr. N. O'Connor) suggest that discharge of high-grade patients would free beds for the lower grade, but low-grade patients can fill these vacancies only if more nurses are provided—and this sets the limit, not the number of beds.

Dr. J. Tizard's chapter on psychological aspects is a positive, though puzzled, attempt to emphasise the future importance of psychologists in planning reablement above and beyond his function as a counsellor and tester. Generally, Dr. Tizard's attacks on certain published views seem justified, and if he feels that his function is to clear the dead wood off the ground he is doing it well. But what does he envisage the role of the psychologist to be? Once the ground is cleared, what will he build there?

Miss E. Williams gives a lively description of that little-known place, the occupation centre, which should be read by all who run or plan such centres. Though her chapter is entitled Education and Training, this topic is in fact dealt with in Dr. O'Connor's discussion of the successful employment of the defective—perhaps the most interesting and forward-looking chapter in the book. He points out that after the establishment of most of our present colonies, following the recommendations of the Wood Committee in 1929, many of them became the stagnant pools we were warned against, and that it is only in the past few years that a system of training and reablement has been coming to be adopted. His own and Dr. Tizard's important work on reablement is very properly described in some detail, with particular emphasis on the importance of the emotional stability of the defective at work.

Dr. O'Connor and Dr. Hilliard do attack "the wide social problem" of mental defects, as the rest of the book scarcely does: but it will certainly be an excellent text and reference book.

Mechanisms of Hypertension

HENRY A. SCHROEDER, M.D., F.A.C.P., associate professor of medicine, and director, hypertension division, department of internal medicine, Washington University School of Medicine. Springfield, Ill: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957. Pp. 379. 67*s*. 6*d*.

Dr. Schroeder's monograph is unusual among recent publications on hypertensive diseases inasmuch as it deals briefly with his clinical experience of this type of illness. He takes a firm stand on the definition of hypertension, considering that a diastolic pressure of over 90 mm. Hg is abnormal, regardless of age; but he produces no new evidence in support of this view.

Thereafter, he develops a fascinating, if tenuous, speculation on the mechanisms responsible for the maintenance of a high blood-pressure; after discarding a number of previous hypotheses, he suggests that abnormalities in the metabolism of trace metals, particularly vanadium, may be intimately concerned. Several very interesting experiments are described, but they do not provide very firm evidence in favour of his hypothesis. The mechanisms of production of atherosclerosis are covered more briefly, and the fashionable dietary fat and fatty-acid theory is supported in principle, though the possible effects of trace metals are again given emphasis.

Treatment is covered briefly and rather didactically; here again, the possible relations between trace metals and hydrallazine are considered, and the use of this drug is encouraged.

Though the book is of much interest to all workers dealing with hypertension, its many heterodox and unproven views detract from its value as a work of reference. The speculation is stimulating and persuasive, but its foundations are uncertain, and there is no doubt that the reader's critical faculties must be on the alert.

A Guide to Blood Transfusion

R. J. WALSH, M.B., Prof. H. K. WARD, F.R.A.C.P. Sydney: for the Australian Medical Publishing Co. 1957. Pp. 164. 20*s*.

IN their preface the authors say, very reasonably, that books on blood-transfusion have now become so complicated that they deter all except specialists. Their own small volume is designed to help the general practitioner and the specialist in other fields who are called upon to give blood-transfusions, and they also address it to medical students. The book is a practical manual with the minimum of theory and no references. The descriptions are clear and properly detailed. Many useful practical points are mentioned about the collecting, giving, and matching of blood. The book can be thoroughly recommended, but it is a pity that it was not produced in a simpler format—say, as a paper-backed pamphlet like the Medical Research Council's memoranda on the same subject. It could then have been sold at a price that would have encouraged people to buy their own copies.

Modern Trends in Neurology

Second series. Editor: DENIS WILLIAMS, C.B.E., M.D., D.SC., F.R.C.P. London: Butterworth. 1957. Pp. 350. 72*s*. 6*d*.

THIS collection of essays by various authors admirably bridges the gap between the results of applied neurological research and the subjects in the textbooks. There are a number of questions which, though at present largely academic, already have important clinical implications. This book enables neurologists to learn something about these matters, and thus encourages the growth of clinical fruit from research work. Its contributors are allowed scope to expand those aspects of their subject which they think important and interesting. Among many good articles, one of the best is Prof. C. E. Lumsden's on myelination and the activity of oligodendrocytes. It illustrates very well the unexpected links which may appear between the seemingly very academic and the clinical.

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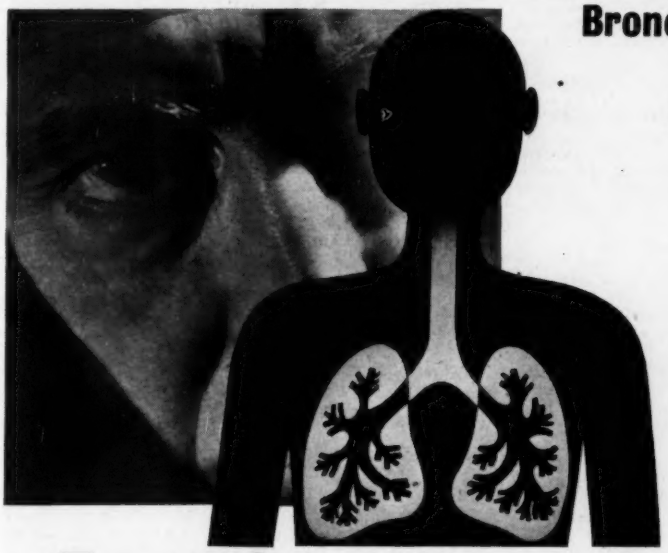

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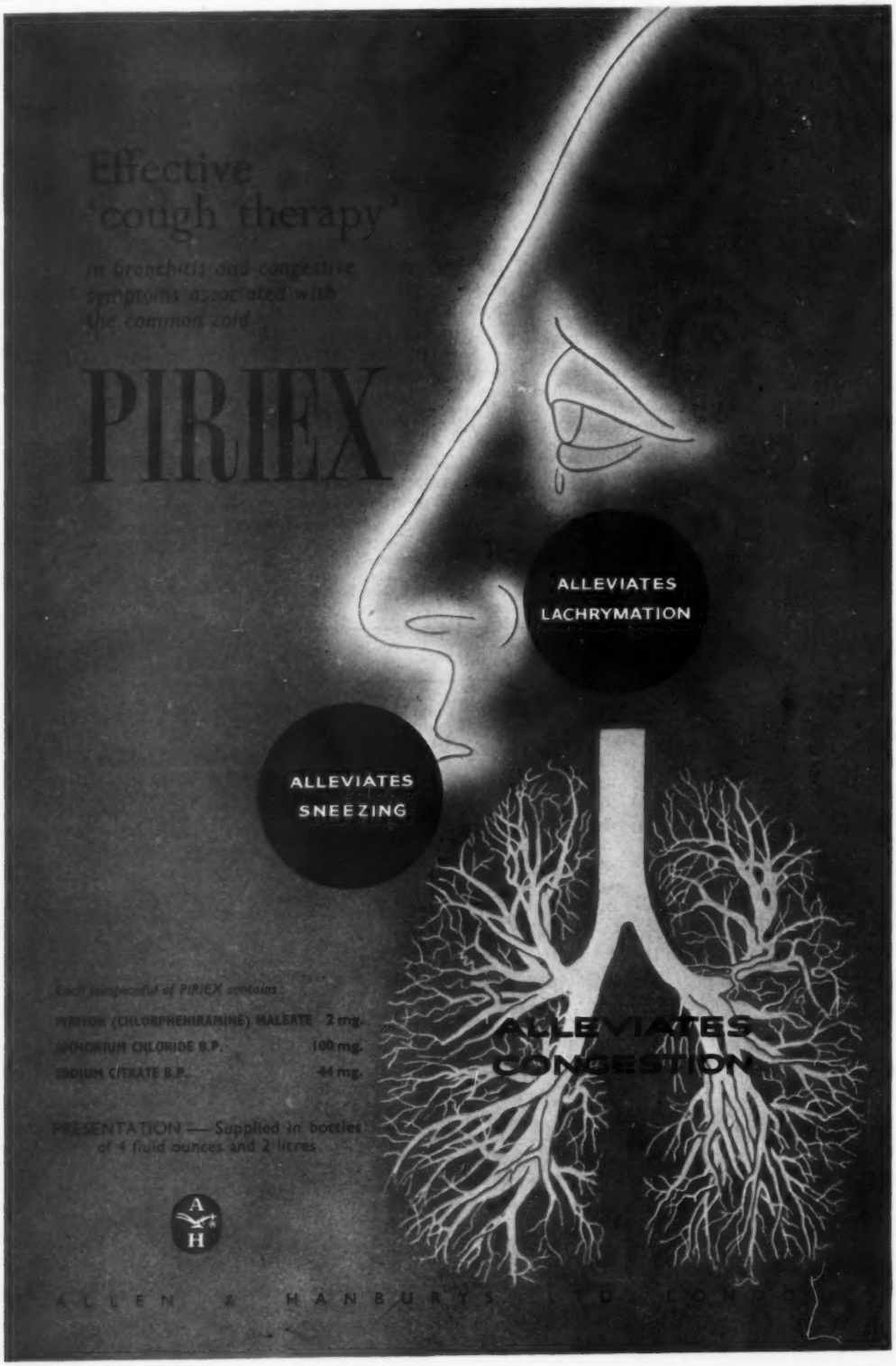
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Sickle-cell Anæmia : a Children's Disease

SORTING out the various forms of hæmoglobin has greatly helped in sorting out the clinical anomalies of sickle-cell disease. This disease was first described in America, and the classical descriptions in the textbooks give the picture of it in the American Negro, usually adolescent or young adult ; in the U.S.A. sickle-cell anæmia is not a disease of infants and young children. WINTROBE [1] states : "There is a record of but six cases of sickle-cell anæmia before six months of age, and only six more in the succeeding age period of six months to one year." The supposed explanation is that at birth only some of the hæmoglobin is the pathological hæmoglobin S ; the full complement is reached only later on, about the time that normal adult hæmoglobin completely replaces fœtal hæmoglobin. The American Negroes come mostly from West Africa, where the disease resembles the American in many respects. It seemed that sickle-cell anæmia did not occur in East Africa ; in 1926 ARCHIBALD [2] recorded a case in the Sudan, but in 1945 TROWELL [3] described the disease in Uganda and in 1951 J. and C. LAMBOTTE-LEGRAND [4] reported 88 patients from the Belgian Congo. The Belgian workers noticed that the disease started at an earlier age and evolved more rapidly than in American Negroes. TROWELL et al.[5] have now published an account of 59 patients with sickle-cell anæmia studied in Uganda, the majority of whom were young children ; 37 cases were diagnosed in the first 2 years of life, 4 under 6 months of age and 16 aged 6–12 months. The disease begins as a mild disorder during, or soon after, the 3rd month of life ; from the age of 6 months its evolution is rapid and many patients die before they are 2 years old.

The reason for this surprising clinical difference is thought to be related, partly at least, to differences in the abnormal hæmoglobins present. NEEL [6] and BEET [7] suggested that sickle-cell anæmia, the severe disorder, was a homozygous condition and the sickle-cell trait, which causes little or no clinical disability, the corresponding heterozygous condition. This hypothesis was confirmed when PAULING et al.[8] demonstrated the abnormal hæmoglobin S in the red cells of affected patients. It was then supposed that the heterozygous person inherited some hæmoglobin S from one parent and normal adult hæmoglobin A from the other, whereas the patient with sickle-cell anæmia inherited hæmoglobin S from both parents; and the high proportion of abnormal hæmoglobin in the red cells was correlated with the clinical manifestations of the disease. In 1951 ITANO [9] and KAPLAN et al.[10] described another hæmoglobin variant which they called hæmoglobin C, and in 1954 SMITH and CONLEY [11] described "sickle-cell hæmoglobin-C disease" in which patients have hæmoglobin C inherited from one parent and hæmoglobin S inherited from the other. Clinically this disease presents as a milder form of sickle-cell disease with later onset and longer expectation of life. Further researches have shown that hæmoglobin C is common in West Africa ; thus EDINGTON and LEHMANN [12] give maps showing how hæmoglobin C is common in the Gold Coast and in Western Nigeria. This contrasts with hæmoglobin S, which has a high frequency in the populations living in a broad belt across Africa south of the Sahara and north of the Zambesi river from the west coast to the east. It is still uncertain how far the clinical picture of sickle-cell disease in America and West Africa is coloured by including patients with hæmoglobin-C sickle-cell disease.

TROWELL et al. have taken advantage of the fact that hæmoglobin C is not found in Uganda to set out in detail the clinical picture of "pure" homozygous sickle-cell anæmia ; the only variant of adult hæmoglobin found in their patients' blood was hæmoglobin S. The disease begins insidiously in infancy, and its onset is often not noticed because the African mothers "regard some degree of ill-health, malaria and 'fever' as a normal feature of infancy". But in 4 children attending a welfare clinic in the Kampala area, mild anæmia with leucocytosis and normoblasts in the peripheral blood were found between the 3rd and 6th month and the diagnosis could then be confirmed by electrophoresis of the hæmoglobin and the appearance of clinical signs. One of the difficulties is that this blood picture is often due to malaria, and malaria superimposed on sickle-cell anæmia has been found ; in such cases a decision about diagnosis has to be postponed until the malaria has been treated. In addition to the anæmia there was usually some intermittent fever, sometimes accompanied by jaundice ; the spleen became palpable in 30 out of 37 children under the age of 2 years, but there was no gross enlargement. The striking and distinctive clinical finding was repeated swelling in the hands and feet due to acute osteopathy ; this was recorded in 11 out of 19 children aged 6–24 months who were attending the welfare clinics. Severe pain and fever are followed in a day or two by swelling, heat, and œdema, over the affected bones ; then the signs slowly subside and after a fortnight only minor thickening and tenderness remain ; some radiographic changes in the affected bones appear after seven to ten days. These attacks of osteopathy were uncommon in children over 2 years old and were never seen in children over 6 years old.

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Between 1 and 6 years, osteopathy of the long bones, with varying degrees of periosteal reaction, was more typical. Another bone sign is bossing of the skull; this is increasingly common in children after their 1st year; it occurred in half the patients aged up to 8 years and in 2 out of 6 adolescents; the bossing is quite easily seen and there are typical X-ray changes.

These observations emphasise that in Uganda sickle-cell disease is predominantly a disorder of childhood. TROWELL et al. had only 6 patients aged 12–18 years and no adults in their series of 59 cases. In the Belgian Congo VANDEPITTE [13] has recorded 261 cases of sickle-cell anæmia; only 10 of the patients were over 10 years old, and only 1 was an adult. The evidence from Uganda and the Congo is that, if the children survive, the disease tends to become less severe and the hæmolytic crises less frequent; the adolescents show a type of physique, with long thin limbs and asthenic build, already recognised as characteristic of "pure" sickle-cell anæmia. But TROWELL et al. believe that the proportion of patients who survive to adult life and can reproduce themselves is very small. The mortality among affected children is indeed high. J. and C. LAMBOTTE-LEGRAND [14] published in 1955 results in a series of 300 cases of sickle-cell anæmia seen in the Belgian Congo; 10 died before the age of 6 months, 62 between the ages of 6 months and 2 years, and after up to 5 years' observation 150 of the patients had died. Despite this grim record, sickle-cell disease persists at remarkably high frequencies in tropical Africa. Two reasons are suggested for this persistence. LEHMANN and RAPER [15] have pointed out that "if the sickling gene (S) had no lethal effect, a population showing 36% of the phenotype S can be calculated to consist of 4% of the genotype SS, 32% of the genotype AS, and 64% of normal persons of genotype AA"; the disease is so fatal only in the 4% of homozygotes SS, whereas the 32% of AS heterozygotes can survive to adult and reproductive life. The second reason is that these AS heterozygotes may actually survive better than the normal AA adults because the AS patients are more resistant to the prevalent malaria. This seems to be due to the fact that the mosquito vector is adapted to utilise normal adult hæmoglobin and finds hæmoglobin S "unpalatable". ALLISON,[16] who proposed this hypothesis, was dealing particularly with *Plasmodium falciparum* infection; and his ideas have been supported by RAPER,[17] though it is far from clear that they apply to all areas.[15 18] TROWELL et al. calculate that about 1% of the children in the vast belt across Africa where hæmoglobin S is found are destined to have sickle-cell anæmia.

Treatment of sickle-cell anæmia in the tropics is difficult and largely ineffective, because it is difficult to obtain the cooperation of parents, who know that survival is problematical. Treatment with acetazolamide ('Diamox'), a carbonic anhydrase inhibitor, has given encouraging results, according to a preliminary report by HILKOVITZ,[19]; and this drug may prove especially valuable since it can be given orally.

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The Glomerulus and the Electron Microscope

OUR knowledge of the elaborate structure of the filtration apparatus in the glomerulus has been expanded greatly by electron microscopy of material obtained mostly by needle biopsies of the kidney. Workers in nearly a dozen different centres throughout the world [1 2] have produced clear evidence that three main elements are concerned in the normal glomerular capillary wall—epithelial cells, basement membrane, and endothelial cells. The epithelial cells are continuous with the capsular epithelium and thence with the tubular epithelium: they are few, but their cytoplasm is thinned out over the whole surface of the loops where it branches into numerous foot processes, which interdigitate with the foot processes of other trabeculæ of the same or neighbouring epithelial cells; the tips of these processes show increased density and lie closely apposed to the basement membrane. The basement membrane is of uniform thickness and almost homogeneous, showing no fibrillar or other type of structure; there is an indefinite layer of slightly less density on each side of the main layer. The endothelial cells are three to four times more numerous than the epithelial cells; their cytoplasm is of greater density than that of the epithelial cells and is abundant only in the region of the nucleus, elsewhere being greatly attenuated along the inside of the capillary loops, where there are apparent interruptions or vesicles within the cytoplasm. No collagen is found in the glomerulus. MUELLER et al.[3] maintain that the capillary stalks in the glomeruli are formed by the main endothelial-cell bodies, while the capillary lumina consist of only the attenuated cytoplasm spiralling around, with their basement-membrane and epithelial-cell coverings—thus denying the existence of the mesangium or intercapillary space.[4–7] Other minor controversial points, such as whether there is a cell membrane or pores [8] between the foot processes of the epithelial cells, and the nature of the vesicles or "pores" in the endothelial cells, may be clarified when they are examined under conditions of physiological stress or of disease.

Several investigators [9] have studied glomeruli in nephrotoxic serum nephritis in laboratory animals, and workers at two centres have reported their findings in human disease. In biopsy material from a patient with diabetes mellitus and clinical evidence of damage to the kidneys, BERGSTRAND and BUCHT [10] found that the hyaline masses (first described by KIMMELSTIEL and WILSON [5]) were within the cytoplasm of the endothelial cells, which had proliferated; there was also focal thickening with hyaline material and folding of the capillary basement membrane, and similar masses were seen between the fibrils of Bowman's capsule; but no definite structure was seen, though some parts suggested the presence of very fine fibrils.

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7. Goormaghtigh, N. *Amer. J. Path.* 1947, **23**, 513.
8. Bergstrand, A. *Lab. Invest.* 1957, **6**, 191.
9. Reid, R. T. W. *Aust. J. exp. Biol. Med.* 1956, **34**, 142. Piel, C. F., Dong, L., Modern, F. W. S., Goodman, J. R., Moore, R. *J. exp. Med.* 1955, **102**, 573.
10. Bergstrand, A., Bucht, H. *Lab. Invest.* 1957, **6**, 293.

BERGSTRAND and BUCHT suggest that this hyaline material is a degenerative feature of the cell cytoplasm due to metabolic changes in the mucoproteins. On this basis, they believe that the capillary basement membrane is part of, or derived from, the endothelial cells. The name "intercapillary glomerulosclerosis" is therefore inadequate.

In an extensive study of renal diseases in children, FARQUHAR et al.[11] examined material (obtained mostly by needle biopsies but sometimes by open surgical biopsy) from sixteen patients with nephrosis, seven with glomerulonephritis, and three with disseminated lupus erythematosus. In the early stages of each of these diseases there were distinctive variations in the glomerular structure, though in the later stages the final pictures of hyalinised glomeruli were very similar. In nephrosis, both familial and non-familial,[12] a constant finding, beautifully illustrated and entirely convincing,[2 11] was loss of the foot processes of the capillary epithelial cells, leaving broad masses of the cytoplasm covering the capillary loops; the severity of this lesion increased with severity of the clinical state. The cytoplasm immediately adjacent to the basement membrane retained the increased density found in normal foot processes at the same situation. Also, the epithelial cytoplasm often showed increased vacuolation and vesicle formation. The endothelial cytoplasm often appeared swollen, with numerous vesicles and a fine meshwork at its luminal boundary, all suggesting increased activity in the transport of fluid. In the majority of cases the basement membrane was somewhat thicker than normal and occasionally had a moth-eaten appearance. In glomerulonephritis the early changes (but not within a month of the onset) were proliferation of the endothelial cells, followed by proliferation of the epithelial cells and reduction of the urinary spaces and capillary lumina, in which mononuclear cells had accumulated; many polymorphs were seen in one case in which clinically there was an acute exacerbation of subacute glomerulonephritis. There was also an accumulation of basement-membrane-like material intimately admixed with endothelial cytoplasm; usually this appeared structureless, but sometimes it was fibrillar or floccular. In the later stages capillary lumina became more and more blocked, the last to be affected being the more peripheral. Ultimately the glomeruli became shrunken to a few atrophic cells and masses of heterogeneous material apparently derived from proliferation of basement membrane. Up to the final disappearance of recognisable epithelial cells the structure of the foot processes was clearly preserved. In disseminated lupus the basement membrane showed increase in thickness, varying in different glomeruli even in one patient; the thickening was most distinct first in the peripheral parts of the loops, but in more severe degrees the whole glomerulus was involved. There was also proliferation of the endothelial cells, again to varying degrees in glomeruli from the same patient; when it was pronounced, the thickening of the basement membrane was nodular as well as general. The epithelial cells were not ordinarily involved in this condition, though in the advanced stages the hyalinisation of the thickened basement membrane and proliferated endothelium produced a picture not unlike that in the final stages of the other two conditions. FARQUHAR et al. point out that changes in the epithelial-cell structure accompany the clinical condition of massive loss of protein from the kidney, while thickening of the basement membrane and proliferation of the endothelial cells are associated with hypertension and azotæmia, and that the severity of the clinical condition corresponds with the severity of the glomerular lesion.

These observations must be confirmed before their clinical significance can be fully evaluated. Meanwhile it is noteworthy that in nephrosis FARQUHAR et al. incriminate primarily the glomerulus and state [2] that the tubular changes are only secondary—an interpretation associated with the names of LÖHLEIN,[13] BELL,[14] DUNN,[15] and others who had not the advantage of electron micrographs with which to localise the lesion.

11. Farquhar, M. G., Vernier, R. L., Good, R. A. *J. exp. Med.* 1957, **106**, 649.
12. Vernier, R. L., Brunson, J. G., Good, R. A. *Amer. J. Dis. Child.* 1957, **93**, 469.

Annotations

RADIATION: FURTHER WARNINGS

WE have referred [16] to the disturbing thyroid radioactivity recorded in the United States, and a further investigation [17] in men and cattle from all parts of the United States has now shown that the intensity of activity from time to time could be correlated with the test firing of nuclear weapons. There is evidence that the radioactivity is caused chiefly by iodine 131 which has been ingested (not, as was previously thought, inhaled). The amounts of radioactivity are said to be "far below those that are expected to cause any observable effects"; but they indicate the possibility of contamination of other tissues and by other elements.

The familiar strontium 90 emits beta rays and is technically hard to assay; cæsium 137, another fission product, emits gamma rays and is easier to estimate, and its concentration is thought to be a direct measure of fallout-rate. The distribution of this isotope has lately been investigated at Los Alamos,[18] and from the amounts found in people and foodstuffs it has been concluded that the element is "unlikely to be a decisive factor in the long-term hazards from weapon-testing and reactor-waste disposal". It accumulates in muscle, not in bone as does strontium 90, which is potentially much more dangerous; but cæsium can be used as an indicator in research on the mechanisms and rate of fallout and stratospheric storage.

Under the auspices of the United States Atomic Energy Commission, a committee of 12 scientists (including Dr. Willard Libby) have reconsidered the hazards from fallout of strontium 90.[19] They believe that fallout is not uniform over the globe but tends to band in the temperate zone of the northern hemisphere where the jet streams flow just below the stratosphere; thus, it is heavy in the northern United States. The committee predict that the strontium 90 so far generated will cause skeletal concentrations of 2–5 strontium units in the north-eastern states if present conditions are maintained, and 4–10 units if the predicted "banding" takes place. The corresponding figures if tests continue at the same rate in "the next several years" will be 5–12 and 10–25 units. (From the calculations of the Atomic Scientists' Association,[20] 10 units might be expected to produce bone sarcoma in about 1 in 20,000 of those affected.)

13. Löhlein, M. *Ergeb. allg. Path. path. Anat.* 1910, **14**, 874; *Ergeb. inn. Med. Kinderheilk.* 1910, **5**, 411.
14. Bell, E. T. *Amer. J. Path.* 1929, **5**, 587.
15. Dunn, J. S. *J. Path. Bact.* 1934, **39**, 1.
16. *Lancet*, 1956, ii, 8.
17. Comar, C. L., Trum, B. F., Kuhn, U. S. G. IIIrd, Wasserman, R. H., Nold, M. M., Schooley, J. C. *Science*, 1957, **126**, 16.
18. Anderson, E. C., Schuch, R. L., Fisher, W. R., Langham, W. *ibid.* 1957, **125**, 1273.
19. *New York Times*, Aug. 26, 1957.
20. See *Lancet*, 1957, i, 878.

Turning to the impact of radiation on the germ cells, a study group of the World Health Organisation has examined its effect on heredity.[21] Their report,[22] which is chiefly concerned with radiation produced for peaceful purposes, recommends the establishment of large institutes for the study of human genetics; and this plea will be echoed by all who have noted, in estimates of the genetic effects of radiation, the many assumptions made at every turn. For example, Glass[23] points out that the doubling-dose of radiation (i.e., the dose to the gonads that would double the incidence of mutations) is unknown and may even be no more than equal to the background dose—in other words, about 3r in 30 years on the average. A year ago the National Academy of Sciences recommended 10r as a permissible gonad dose, on the assumption that this was not more than a quarter of the doubling dose; but if 10r is really three times the doubling dose, the recommendation should be radically revised. Intensive research is clearly needed. Glass also remarks that, since mutations are caused by the fracture of a chromosome followed by reunion of the broken ends in a new pattern, at least two fractures are needed for a mutation; this is why the incidence of mutations increases as the square (or some higher power) of the dose. But though mutations are rare at low doses, it is very unlikely that there is any threshold below which no damage is done. There is no experimental evidence of a threshold, and theory leads us to expect that there is none. The W.H.O. group affirm that "all man-made radiation must be regarded as harmful from the genetic point of view." In this respect, we believe, weapon-testing should be distinguished from other uses of nuclear energy; continued explosions cannot be justified by comparing their consequences with the much more controllable hazards involved in the construction and running of atomic power stations.

ERGONOMICS

DESIGNING an aeroplane cockpit calls for knowledge of bodily dimensions and of the posture that can be maintained most easily without fatigue. In addition the pilot must be protected against heat and cold and oxygen lack; he must be enabled to see around him; he must be supplied in a clear way with the information needed for control of the aircraft, with attention to the size and position of dials and their relation to each other, the size and shape of letters, numbers, and pointers, and the illumination of these instruments; and lever and controls must be suitably placed. In the study of such elements physiologists, anatomists, anthropologists, psychologists, and design engineers are all concerned.

A new quarterly journal, devoted to "human factors in work, machine control, and equipment design" bears the title *Ergonomics*[24]—a word (not to be found in the Oxford English Dictionary) which the journal itself defines as "the customs, habits, or laws of work". Since the late war the results of ergonomic research have been applied increasingly in industry; but progress has been impeded by the scattering of relevant reports throughout many different specialised journals.

The eight articles in the first issue of *Ergonomics*, which has an international board of editors, include contributions from America, Germany, and Holland. In an article of interest to all car-drivers R. A. McFarland examines the problems of vehicle design. Members of the Harvard School of Public Health undertook anthropometric measurements on 370 lorry and bus drivers, which were used in assessing different vehicles; and in one of these vehicles it was shown that tall drivers could not operate the footbrake when the gear lever was in certain positions.

McFarland concludes that "the efficient and safe operation of motor vehicles is a function of the design of the equipment in relation to the characteristics of the operators." Any machine operated by man, he insists, can be regarded as an extension of man's sense-organs and limbs. Once this concept is accepted, it is clear that the design of a machine should be from man outwards. Indeed, wartime research showed that it was better to design equipment within the limits of human capacity than to try to match men to the demands of machines by selection and training.

ELECTROLYTES DURING LABOUR

MANY investigators have demonstrated metabolic changes suggestive of increased adrenocortical activity in association with trauma, burns, acute illness,[1–3] and, surgical operations.[4] Labour is a form of injury, and especially when long-continued, it [4] may give rise to metabolic disturbances.

In a study of blood-electrolytes in long labour Hawkins and Nixon [5] have shown, among other significant changes, a consistent loss of plasma-water and increase in plasma-specific-gravity after only twenty hours' labour, indicating a state of dehydration long before clinical signs of this are present. This evidence supports the widely held belief that absorption from the intestinal tract is grossly disturbed during labour lasting more than a few hours, and is often inadequate to ensure normal hydration and essential nourishment. There is little point in forcing solid food or extra fluids by mouth once labour has lasted more than twenty-four hours; for the material will often not be absorbed and will merely encourage vomiting, thus increasing the risk of inhalation of stomach contents if anæsthesia has to be induced. Fluids should be given by intravenous infusion if delivery is not imminent after twenty-four hours in labour.

Other important findings by Hawkins and Nixon were an increase in plasma-sodium and a decrease in chlorides and potassium. They suggest that increased renal excretion of chlorides may maintain the acid-base balance, which is disturbed by the ketosis that commonly follows shortage of available glycogen. Glucose should therefore be added to the parenteral fluid. Hawkins and Nixon recommend isotonic combinations of 4·3% glucose and 0·18% sodium cloride; concentrations of glucose up to 10% are used successfully by many obstetricians.

After forty-eight hours in labour the plasma-potassium level and eosinophil-count fell strikingly. These changes, consistent with increased activity of the adrenal cortex, are similar to those following surgical operations [4] and have been reproduced experimentally by giving corticotrophin daily.[6] The fall in the level of plasma-potassium may be especially important in labour because of its influence on muscular contraction. In experiments isolated strips of uterine muscle lose much of their power of contraction when the potassium in the surrounding medium is reduced, and the stimulus needed to produce the contraction increases.[7] Potassium depletion in labours lasting forty to fifty hours may well contribute materially to the inefficiency of an already inert uterus and prolong labour further. Progress in labours of such duration is not always continuous, but is sometimes apparently delayed for many hours at about the same degree of cervical dilatation. It will be interesting to learn whether

21. *ibid.* p. 697.
22. Effect of Radiation on Human Heredity. World Health Organisation, Geneva. 1957. Pp. 168. 20*s*. Obtainable from H.M. Stationery Office, P.O. Box 569, London, S.E.1.
23. Glass, B. *Science*, 1957, **126**, 241.
24. *Ergonomics*, official publication of the Ergonomics Research Society. General editor: A. T. Welford, Psychological Laboratory, Downing Place, Cambridge. Published by Taylor & Francis Ltd., Red Lion Court, Fleet Street, London, E.C.4. £4 15*s*. per vol.; £1 5*s*. per part.

1. Selye, H. Stress. Montreal, 1950.
2. Brown, M. R., Currens, J. H., Marchand, J. F. *J. Amer. med. Ass.* 1944, **124**, 545.
3. Darrow, D. C., Pratt, E. L. *ibid.* 1950, **143**, 365, 432.
4. MacPhee, I. W. *Brit. med. J.* 1953, i, 1023.
5. Hawkins, D. F., Nixon, W. C. W. *J. Obstet. Gynæc., Brit. Emp.* 1957, **64**, 641.
6. Prunty, F. T. G. *Brit. med. J.* 1953, i, 852.
7. Csapo, A. *Rec. Progr. Hormone Res.* 1956, **12**, 405.

the correction of electrolyte disturbance by administering appropriate quantities of deficient electrolytes (for example, in a modified Ringer solution) influences the course of labour due to disorderly uterine activity.

CORTISONE v. ASPIRIN AGAIN

THE Empire Rheumatism Council's multi-centre controlled trial comparing cortisone and aspirin in the treatment of rheumatoid arthritis has ended its third and last year, and a final report has been published.[1] At the outset of the trial treatment was started in 100 patients, of whom 50 received cortisone and 50 aspirin. Patients with gross irreversible damage in their joints or outside the age range 17–60 were not accepted. In all patients aspirin or cortisone was used to supplement a planned régime of general care, including the use of splints and physiotherapy. Of the 100 starters 53 reached the three-year finishing-post—29 cortisone cases and 24 in the aspirin group. What of the remainder? 5 of the aspirin cases fell out because of dyspepsia, and 8 because they were deteriorating or because a change of treatment was deemed necessary; 10 more stopped attending. Treatment with cortisone was stopped in 8 cases because of undesirable effects, and in 9 because of deterioration or because it was considered desirable to change the method of treatment; only 2 cases in this group stopped attending. The undesirable effects of treatment with cortisone included hypertension in 2 cases, and single examples of severe headache, tuberculosis, psychosis, œdema, and perforated peptic ulcer. The total daily dose of cortisone was 75 mg. at the beginning, and this was adjusted later to individual needs—treatment being abandoned, however, if 100 mg. or more daily was needed to produce an acceptable measure of symptomatic relief. In the third year only 1 patient was able to stop taking cortisone because of an apparent remission.

As in the earlier stages of the trial[2] (and in a rather similar comparison of the same two agents in early rheumatoid arthritis[3]) there was strikingly little difference between the response to aspirin and to cortisone. Subjective well-being was maintained slightly better in patients treated with cortisone, but the two groups did not differ in their capacity for work. At the end of the first year cortisone and aspirin cases alike showed an improvement in function, but thereafter there was little change in this regard. There was a similar trend in the number of joints affected. The erythrocyte-sedimentation rate in the two groups, after diverging in the first two months (when the rate fell sharply in cases treated with cortisone), had converged at the end of the first year, and thereafter showed little change or difference, except for a slight deterioration in the third year in the cortisone group. Changes in hæmoglobin conformed to the same pattern. Radiographs at the beginning and end of treatment were scrutinised and extension of articular damage was recorded. Analysis of changes in the radiographic appearances of the hand and wrist showed that both groups were similar initially, that both showed comparable worsening, and that a comparable number of new joints became affected in the first year. By the end of the second year further deterioration had occurred in both groups, slightly more in the aspirin than in the cortisone group, though the difference reached significant levels according to only one out of several methods of scoring. At the third year there were not sufficient films for valid comparison, but there was no difference between the groups in those still available for study. The method of scoring was not designed to take radiographic improvement into account; but such improvement, striking in extent, was apparent in 2 cases, both treated with cortisone.

1. Empire Rheumatism Council. *Ann. rheum. Dis.* 1957, **16**, 277.
2. Empire Rheumatism Council. *ibid.* 1955, **14**, 353.
3. Medical Research Council and Nuffield Foundation. *Brit. med. J.* 1955, ii, 695.

How should this report be interpreted by the practising clinician? Despite the similar results of other trials, and the earlier reports of the Empire Rheumatism Council's investigation, cortisone (or related steroids) are being used extensively in the treatment of rheumatoid arthritis. Controlled trials have to be designed to answer specific questions, and criticisms of the questions selected are rarely lacking. The cases included in the Empire Rheumatism Council's investigation were selected only in so far as they satisfied certain broad criteria of age, reversibility of joint changes, and absence of conditions likely to be exacerbated by cortisone. The soundest reason for using cortisone in rheumatoid arthritis is that a group of cases exist which fare very much better on cortisone than on aspirin; but this group is so small that its representation in a trial such as that by the Empire Rheumatism Council would not materially weight the results in favour of cortisone. Clinical impression can readily supply a list of criteria by which cases peculiarly suitable for cortisone can be selected. Clinical impression is, however, fallible and the position must be critically appraised before the evidence of carefully controlled trials is set aside, and treatment with cortisone is given an undisputed place in the therapy of rheumatoid arthritis. The report of the Empire Rheumatism Council, in reviewing the patients who were still having cortisone at the end of three years, remarks with some force that "if one type of patient more than another is to derive benefit from cortisone, as has been alleged, this is the group that should show it". In the event this special benefit could not be demonstrated. The report also comments that the "side-effects" of effective cortisone dosage are undoubtedly more severe and more numerous than those of aspirin. Finally it would be wise not to regard all the conclusions reached in this trial as applicable to prednisone or prednisolone, which must be appraised on their own merits.

HEPATIC CYTOLOGY

BLIND needle biopsy of the liver has become established since Roholm and Iversen[1] reported the first large series in 1939. It has been used not only for the differential diagnosis of hepatic disease but also to study prognosis and response to treatment[2] and in attempts to correlate structure and function. Waldenstein et al.[3] found quite a close association between liver-cell damage and positive serum-flocculation tests, and between scarring and ascites with a low serum-albumin. They concluded that the microscopic appearances of the liver were not an accurate guide to prognosis. It has been suggested that perhaps the main value of blind liver-biopsy is in distinguishing between "medical" and "surgical" jaundice.[4] In about 15% of cases this differential diagnosis can be very difficult; but even biopsy does not always solve the problem; at a recent symposium[5] on intrahepatic cholestatic jaundice the panel, which contained Dr. H. Popper and Dr. Hoffbauer, admitted a high failure-rate. The technique has been used to establish such diverse diagnoses as hæmochromatosis, Gaucher's disease, the granulomatoses (including sarcoidosis,[6] tuberculosis, brucellosis, and leprosy), fungal infections, infective mononucleosis, leptospirosis, hepatitis, lymphoma, polyarteritis nodosa, and certain parasitic infections. Clinical diagnosis of liver-disease may also need to be revised as a result of liver-biopsy in as many as half the cases.[7] Schiff[2] found liver-biopsy of particular value in excluding liver disease in the presence of abnormal liver-function tests, differentiating "medical" from "surgical" jaun-

1. Roholm, K., Iversen, P. *Acta path. microbiol. scand.* 1939, **16**, 427.
2. Schiff, L. *Ann. intern. Med.* 1951, **34**, 948.
3. Waldenstein, S. S., Popper, H., Szanto, P. B., Steigman, F. *Arch. intern. Med.* 1951, **87**, 844.
4. *Lancet*, 1954, i, 612.
5. American Society for the Study of Liver Disease, 1957.
6. Mather, G., Dawson, J., Hoyle, C. *Quart. J. Med.* 1955, **24**, 331.
7. Christian, E. R. *Amer. J. Med.* 1952, **13**, 689.

dice, evaluating the response to treatment, elucidating obscure hepatomegaly, differentiating intrahepatic from extrahepatic portal-vein block, diagnosing the granulomatoses, and searching for secondary neoplastic deposits.

Despite the many large series of needle biopsies of the liver reported, some still look on it with misgiving and think it unduly hazardous for a diagnostic procedure. Terry [8] collected over 10,600 biopsies from the literature and added over 200 of his own. 13 deaths were reported—11 from hæmorrhage, 1 from biliary peritonitis, and 1 from shock—but most of these deaths were before the contraindications were realised and would therefore have been avoided in later series. Terry correlated hæmorrhage directly with the size of the biopsy needle. Needles with a bore of more than 2 mm. seemed distinctly dangerous, and should not be used. In an even larger series Zamchek et al.[9] also found that the mortality was in the order of 1 per 1000 biopsies.

As far as possible, biopsy should be done only by those experienced in it. The most obvious contraindication is a hæmorrhagic diathesis, from either prothrombin lack (so common in liver disease) or some other deficiency; and severe congestive failure also increases the risk of hæmorrhage from the puncture site. Almost as great are the risks resulting from leakage of bile from an obstructed duct; several deaths from this cause have been reported.[10 11] Biopsy may cause infection to spread, particularly from cholangitis or subphrenic or hepatic abscess; and in the presence of amœbiasis or hydatid disease biopsy should be avoided. According to the route of approach—transpleural or subcostal—local disease of the pleura or right lower lobe or of the peritoneum may make needling unwise. Thus in many patients, despite the need for biopsy, it may be unsafe to proceed. The introduction of a safer technique would be of great advantage.

Such a technique has been described by Espinoza et al.[12] in the University of Chile. They have studied smears of hepatic tissue made by direct aspiration from the liver with an ordinary large intramuscular needle (preferably with a trocar) and a dry sterilised syringe. The needle is heparinised and introduced into the liver, the trocar is withdrawn, and strong suction is applied with the syringe; a few drops of bloody material are obtained from which smears can be made for direct cytological study. Wright-Giemsa stain was found to be the most suitable for routine use. If cancer is suspected the liver can be safely punctured in several places, and local anæsthesia does not appear to be essential. Espinoza et al. found that in fifty-one punctures on 41 patients there was no morbidity, and the only contraindications were hydatid disease, or disease of the right lung or pleura if the transpleural approach was used. No patient refused a second puncture. The hepatic smears showed that 4 livers were normal, 2 had obstructive jaundice characterised by normal cells with much intracellular and extracellular pigment, 3 had hepatitis (the cells had normal nuclei but basophilic changes and vacuolation of the cytoplasm), 12 had primary or secondary cancer, 3 were fatty, 1 had hæmochromatosis, and 16 had cirrhosis. Here the characteristic change is a very large nucleus with condensed chromatin and a prominent nucleolus; pigment may be present in the cytoplasm, which is basophilic and vacuolated. Further studies by these workers on 44 more patients (personal communication) have confirmed their earlier observations, the only difficulty encountered being in the distinction between primary biliary cirrhosis and obstructive jaundice.

If these claims for simplicity and safety are confirmed the technique may well be of value, particularly where biopsy is otherwise contraindicated. The method seems to have much to recommend it in the search for neoplastic deposits, if multiple puncture can indeed be performed safely, and in the diagnosis of hæmochromatosis, where a single smear stained for iron should give the answer. But the method demands a skilled cytologist to interpret the smears, and care and experience are needed to attain the accuracy necessary for the technique to become accepted.

MESENTERIC EMBOLECTOMY

Morris [1] has named aggressiveness in the surgeon as one of seven criteria for improved results in mesenteric vascular occlusion. Occlusion of the superior mesenteric artery results in massive mesenteric and intestinal infarction, and Morgan Williams [2] has suggested that it may be better to attempt nothing further on finding at laparotomy such an extensive lesion. (Occasionally, he says, the intestine recovers of its own accord; but this must be rare good fortune.) Resection of all but a few inches of small intestine, though feasible, is hardly permissible in view of the subsequent crippling, and possibly fatal, nutritional disability. It is nevertheless surgical aggressiveness that is now providing a more hopeful course. When embolectomy in the treatment of occlusion of the superior mesenteric artery was first undertaken by Klass [3] the patient died owing to ventricular failure, but the vessel had been effectively cleared, leaving the intestine viable. Klass relieved infarction in a second patient,[4] who died as a result of postoperative bleeding from mesenteric veins damaged in the approach to the artery. Now Shaw and Rutledge [5] describe the case of a patient who survived this operation.

Success in embolectomy does not depend on surgical technique alone. The embolic event is marked by an initial attack of abdominal pain, sometimes no more than transitory colic associated with a loose motion, which is followed by a deceptive period of clinical quiescence. The preoperative diagnosis is more easily, and therefore more often, made at a later stage when signs of gangrene of the bowel develop; this is clearly not early enough if the patient is to benefit from embolectomy. Sudden abdominal pain causing temporary collapse, soon followed by a watery and possibly bloody stool, in a patient aged 40 or more with cardiac or vascular disease, is an indication for laparotomy [6] even though some hours of tranquillity may have ensued. During those hours there may be no sign, except perhaps tenderness in the right iliac fossa, to indicate an intra-abdominal catastrophe; even gut sounds are audible since the intestine contracts after the embolism. Surprisingly, intestinal vitality persists for some hours, and Klass [4] has removed an embolus of fourteen hours' duration in a patient whose bowel was subsequently found at necopsy to be normal. Shaw and Rutledge performed arteriotomy in a 54-year-old woman twenty-five hours after the embolic event. After the vessel had been cleared, all but a few areas of the bowel became pink; pulsation, though present in the proximal arcades, could not be felt along the mesenteric border of the bowel; and, since it was uncertain which dusky areas would eventually prove viable, the abdomen was closed. Heparin was administered, though Klass has advised against this.[4] Laparotomy was undertaken the next day in order to review the bowel and resect residual necrotic areas if necessary; none were found. Here was most effective surgical aggressiveness.

8. Terry, R. *Brit. med. J.* 1952, i, 1102.
9. Zamchek, N., Sidman, R. L. *New Engl. J. Med.* 1953, **249**, 1020.
10. Rubenstone, A. I., Mintz, S. S., Meranze, D. R. *Ann. intern. Med.* 1952, **36**, 166.
11. Brown, C. Y., Walsh, G. C. *ibid.* p. 1529.
12. Espinoza, J., Meza, C., Orrego, H., Nijamkin, A. *Rev. méd. Chile*, 1956, **84**, 337.

1. Morris, W. R. *Med. Ann. D.C.* 1955, **24**, 12.
2. Morgan Williams, H. *Brit. med. J.* 1946, ii, 856.
3. Klass, A. A., *Ann. Surg.* 1951, **134**, 913.
4. *J. int. Coll. Surg.* 1953, **20**, 687.
5. Shaw, R. S., Rutledge, R. H. *New Engl. J. Med.* 1957, **257**, 595.
6. Johnson, C. C., Bagenstoss, A. H. *Proc. Mayo Clin.* 1949, **24**, 649.

Special Articles

CARCINOMA OF THE CERVIX AT CHELSEA HOSPITAL FOR WOMEN 1933-56

FIVE-YEAR RESULTS OF TREATMENT 1933-51

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THE Chelsea Hospital for Women and the Royal Marsden Hospital * have (since 1944) conducted a Joint Clinic to which most of the patients suitable for radiotherapy are referred. This clinic has grown steadily and satisfactorily, and we believe that it provides a good example of the advantage to the cancer patient of cooperation between surgeon and radiotherapist.

A report covering the early years 1944–46 has already been published (Blaikley et al. 1952). We survey here the patients treated in 1933–56 and compare the results of treatment of carcinoma of the cervix in the period before the formation of the Joint Clinic (1933–43) with those obtained since (1944–51). Cases of cervical-stump carcinoma and carcinoma with associated pregnancy are reviewed separately. Carcinoma in situ, though mentioned, is not considered here in any detail.

Before 1944 surgery was the treatment of choice for carcinoma of the cervix, but patients unsuitable for operation were treated with radium at the Chelsea Hospital for Women by the surgeons without consultation with a radiotherapist; but, at the discretion of the surgeons, some patients were referred for X-ray treatment. Since the Joint Clinic was established in 1944, new patients are seen by both surgeon (J. B. B.) and radiotherapist (M. L.) together, and most of the new cases (83%) at the Chelsea Hospital for Women are referred to this clinic. Radiotherapy is given to these patients at the Royal Marsden Hospital, but if the number of cases is excessive, some of the radium insertions are undertaken at the Chelsea Hospital for Women. In most cases the patient is examined under anæsthesia, when the growth is staged clinically, a biopsy taken, and the final decision made as to the exact form of radiation treatment. Any decision necessitating a change in the plan of treatment is taken only after full consultation between surgeon and radiotherapist.

* Until recently the Royal Cancer Hospital.

At the Joint Clinic, radiotherapy is regarded as the method of choice for treating nearly all cases of carcinoma of the cervix. The main indications accepted for surgery are:

(1) Recurrence after radiotherapy.
(2) Impracticability of adequate radiotherapy because of: (*a*) anatomical abnormality preventing accurate insertion of radium, (*b*) pelvic sepsis, and (*c*) other tumours in the pelvis which require surgery.

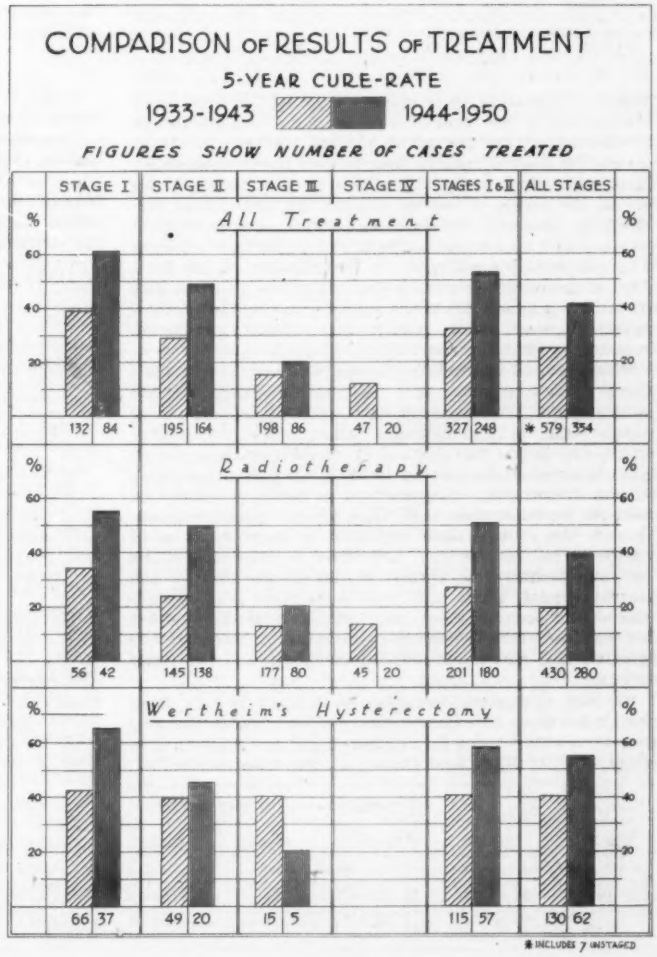
The mainstay of radiation treatment is radium therapy, X-ray therapy being used chiefly as a supplementary method.

Treatment

In principle, patients in stages I and II are treated with radium, a modified Stockholm technique being used, followed by supplementary X-ray therapy directed to the outer parts of the parametria and the side walls of the pelvis. Usually three radium treatments are given, the second a week after the first, and the third two weeks after the second. In stages III and IV cases X-ray therapy is applied before radium is used, and also when the carcinoma is bulky, fungating, or hæmorrhagic, the purpose being to shrink the growth and to control bleeding before embarking on the radium treatment.

Radium Technique and Dosage

In most cases 50–60 mg. of radium is inserted into the uterine cavity and 30–70 mg. into the vagina. In all



cases the uterine source fills the length of the cavity and the vaginal sources completely cover all the disease in the vault. At the same time as much radiation as possible is directed towards the side walls of the pelvis by using as large packets as possible with maximum distension laterally of the vaginal vault. Healthy tissues are protected by securely packing the radium in position.

At the Royal Marsden Hospital, the Manchester point A and B system is not used, because it cannot be applied to the highly individualised Stockholm technique which with its variable radium sources and wide range of differing radium applicators, gives rise to a set of technical conditions which are the exact opposite to those on which the Manchester dosage system depends—i.e., the system of units of radium contained in special apparatus. It is, therefore, impracticable to prescribe dosage in terms of point A when using our Stockholm technique and equipment.

In these circumstances, information has to be obtained about the radium dosage delivered at each treatment for each patient. Fortunately it is possible, by using radiographic localisation techniques, to obtain the necessary information in the form of a single-plane radium dosage distribution within the given patient's pelvis, whatever the combination of radium sources used (Lederman 1954). These individual distributions can be summated at the end of the series of radium treatments and a final distribution obtained showing the 6600r isodose surface within which all neoplastic tissue can be assumed to have been adequately irradiated. A distribution of this kind gives a reasonably accurate picture of the position and extent in a given pelvis of the zone embracing the cervicovaginal disease which requires no further irradiation from any external sources that may be subsequently used.

TABLE I—CARCINOMA OF THE CERVIX IN 1933–56

—	Patients seen	Treated	Not treated
New patients:			
1933–43 ..	596	579	17
1944–51 ..	437	421	16
1952–56 ..	372	368	4
Total ..	1405	1368	37
Recurrent cases:			
1944–56 ..	54	40	14

To determine the radium dosage received by the peripheral pelvic tissues and the neighbouring normal viscera, direct measurement with a scintillation counting system can be undertaken. Since 1949 the dosage within the pelvis has been read directly with a probe-type dose-meter (Lederman 1950) in all patients at each radium treatment. No attempt is made routinely to measure the dose received by the cervicovaginal neoplasm because the dose in this region is so high as to be of academic interest only. Attention is focused on the outlying pathways of spread of the disease and on the healthy tissues, which must not be damaged. The points selected for measurement are: the base of the bladder and both ureteric openings; the anterior wall of the rectum; and the inner and outer limits of both parametria.

Bladder and rectal complications have almost been eliminated since this instrument has been used. Experience shows that these do not develop if the bladder dose remains below 6000r and the rectal dose below 4000r.

TABLE III—HISTOLOGY 1944–56

Histology	New cases	Recurrent cases	Total
Squamous carcinoma ..	651	27	678 (78·6%)
Anaplastic carcinoma ..	68	6	74 (8·6%)
Adenocarcinoma	49	5	54 (6·3%)
Adeno- and squamous carcinoma	3	0	3 (0·3%)
Not confirmed	38	16	54 (6·3%)
Total	809	54	863

X-ray Technique

Armed with the information derived from the radium distribution and the direct pelvic measurements, supplementary X-ray therapy can be given accurately to the areas ineffectively irradiated by radium. With X rays at 250–400 kV, tumour doses of 3000–4000r can be given in 4–6 weeks without severe systemic reactions or high rate of complications.

Patients in stages III and IV receive X-ray therapy first, applied to the whole pelvis. Subsequently radium is used in modified amount according to the response to treatment.

Material

Table I lists all cases seen in 1933–56, and tables II and III all cases seen from 1944–56 are briefly reviewed in relation to age-incidence and tumour histology.

In 1944–48 there were no patients aged less than 30; in 1949–56 there were 17, of whom 5 were seen in 1954. The rising incidence of cervical carcinoma in young patients is quite striking and is shown in table II.

Histology 1944-56

A biopsy specimen is taken from the cervix as a routine before treatment whenever possible. In an exsanguinated unfit patient X-ray treatment is given first and biopsy may be delayed until the radium insertion or the patient becomes fit for examination under anæsthesia. Serial biopsies during treatment have been undertaken during recent years, but it is difficult to know what significance to attribute to the information so derived.

TABLE IV—STAGE-DISTRIBUTION OF TREATED PATIENTS

—	1933–43	1944–51	1952–56
Stage I	132 (23·0%)	97 (23·0%)	100 (27·2%)
Stage II	195 (34·0%)	192 (45·6%)	155 (42·1%)
Stage III	198 (34·0%)	101 (24·0%)	80 (21·7%)
Stage IV	47 (8·0%)	31 (7·4%)	33 (9·0%)
Unstaged	7 (1·0%)	—	—
Total	579	421	368

In 27 cases treated in 1944–51 the biopsy was inadequate for diagnosis. 1 patient (stage II) has survived nine years; 3 patients with stage-III disease and 1 with stage-IV disease died of intercurrent disease within four years. The remainder all died of carcinoma within five years.

Staging

The attempt was made to stage all the cases according to the international method adopted in 1950 (Heyman 1955). The staging in the three series shown in table IV is not strictly comparable in spite of reviewing the 1933–43 cases; in particular, some cases in the 1944–56 group which formerly would probably have been placed in stage III are placed in stage II under the strict interpretation of the international staging.

TABLE II—AGE-DISTRIBUTION OF 809 NEW CASES IN 1944-56

Age (yr.)	20–30	31–40	41–50	51–60	61–70	71–80	81–90	More than 90	Total
1944–1951 ..	4 (0·9%)	50 (11·4%)	91 (20·8%)	134 (30·7%)	115 (26·3%)	35 (8·0%)	8 (1·8%)	0	437
1952–1956 ..	13 (3·5%)	62 (16·7%)	86 (23·1%)	98 (26·3%)	80 (21·5%)	28 (7·5%)	3 (0·8%)	2 (0·5%)	372
Total ..	17 (2·1%)	112 (13·9%)	177 (21·9%)	232 (28·7%)	195 (24·1%)	63 (7·8%)	11 (1·4%)	2 (0·2%)	809

TABLE V—NEW PATIENTS NOT TREATED 1944–51

Stage	Number	Reason
I	0	Nil
II ..	3	All refused treatment
III ..	1	Refused treatment
IV	12	1 died before treatment was started; 1 unfit; 1 refused; in 9 the cancer was too advanced

Untreated Cases

It is exceptional for a patient with advanced cancer of the cervix not to be offered some form of treatment even though purely palliative. Refusal to accept treatment or a moribund patient are the usual reasons for not giving treatment. In 1933–43, 16 patients were untreated because of advanced disease, and 1 patient with stage-II cancer refused, whilst as shown in table V, in 1944–51 16 patients were untreated, but only 9 of them because of the advanced stage of the cancer.

Results of Treatment

Tables VI–IX show the results of treatment in the years 1933–43, and tables X–XIII the results obtained after setting up the Joint Consultation Clinic (1944–51). The results for both periods are compared in the accompanying figure.

TABLE VI—RESULTS OF ALL TREATMENTS 1933–43
(596 patients seen, 579 treated)

Stage	No. seen	No. treated	Alive for 5 yr.	Lost in 5 yr.	5-yr. survival-rate	Absolute survival-rate
I ..	132	132	51	22	38·6%	38·6%
II ..	196	195	54	18	27·7%	27·6%
III ..	198	198	30	18	15·2%	15·2%
IV ..	63	47	6	1	12·8%	9·5%
Unstaged	7	7	1	1	—	—
I and II	328	327	105	40	32·1%	32·0%
All ..	596	579	142	60	24·5%	23·8%

Tables IX and XIII show the results of treatment other than Wertheim's hysterectomy or radiotherapy. These include cases operated on for conditions other than carcinoma when the diagnosis of malignancy was not made until histological examination. In 1944–51 there were also 3 anterior exenterations and 1 total exenteration following radiotherapy; these are included in table XIII. The other treatments are too numerous to list individually but include 5 cases of hysterectomy and bilateral salpingo-oöphorectomy followed by radiotherapy, and 3 cases of radiotherapy and bilateral iliac lymphadenectomy. Pelvic exenterations are done at Chelsea Hospital for Women mainly for recurrent carcinoma, and often where the primary treatment has been given elsewhere. In 1944–51 16 exenterations were done, 9 total and 7 anterior. Only 3 of these patients with total exenteration survived 5 years.

TABLE VII—RESULTS OF RADIOTHERAPY 1933–43
(430 cases)

Stage	No. treated	Alive for 5 yr.	Lost in 5 yr.	5-yr. survival-rate
I	56	19	9	33·9%
II	145	34	12	23·5%
III	177	24	17	13·6%
IV	45	6	1	13·3%
Unstaged ..	7	1	1	—
I and II ..	201	53	21	26·4%
Unstaged ..	430	84	40	19·5%

Radiotherapy

The results of radiotherapy in 1933–43 were bad and are a direct reflection on the poor technical standard of radium therapy then existing and the complete lack of correlation between radium and X-ray therapy. The results of surgery were considerably better than those obtained by radiotherapy, 40·9% against 26·4% for stages I and II. The results of Wertheim's hysterectomy were reasonable for that time.

The period 1944–51 was characterised by a very great improvement in the radiotherapy results, the survival-rates being doubled from 19·5% to 38%. In the same period the surgical results also improved (from 40·8% to 53·5%) but to a much less striking extent—e.g., in stage I and stage II radiotherapy results increased from 26·4% to 51·2%, whereas in the same period the results of Wertheim's hysterectomy for the same stages improved from 40·9% to 56·1%.

TABLE VIII—RESULTS OF WERTHEIM'S HYSTERECTOMY 1933–43
(130 cases)

Stage	No. treated	Alive for 5 yr.	Lost in 5 yr.	5-yr. survival-rate
I	66	28	11	42·4%
II	49	19	6	38·8%
III	15	6	1	40·0%
I and II ..	115	47	17	40·9%
All	130	53	18	40·8%

One feature of the radiotherapy results is, on the surface, disturbing and merits special comment—namely, the relatively low survival-rate in stage-I cases (1944–51). The 60·4% survival-rate obtained in stage-I cases is considerably below the 70% (or better) rate reported by other centres. A detailed analysis of our stage-I cases gives the following information:

(1) There is a definite selection of stage-I cases for radiotherapy. Thus, of 97 cases seen in 1944–51 only 48 were treated primarily by radiotherapy. Many of these patients were referred only because they were unsuitable for radical surgery because of age, general condition, or the anaplastic nature of the tumour.

TABLE IX—RESULTS OF TREATMENT OTHER THAN A RADIOTHERAPY OR WERTHEIM'S HYSTERECTOMY IN 1933–43
(19 cases)

Stage	No. treated	Alive for 5 yr.	Lost in 5 yr.	5-yr. survival-rate
I	10	4	2	..
II	1	1	0	..
III	6	0	0	..
IV	2	0	0	..
All	19	5	2	26·3%

(2) Of the 48 cases treated by radiotherapy 13 (27%) were not referred to the Joint Clinic until after some part of their radiation treatment had already been given. In this group there were only 5 survivors after five years—i.e., 38·4% (cf. 38·6% for 1933–43). Of the remaining 35 patients who were treated from the outset by the Joint Clinic, 24 survived for five years—i.e., 69%, which compares well with 65% obtained by Wertheim's hysterectomy. Of the 11 patients who died in less than five years 4 died of intercurrent disease and 7 of cancer. In all these 7 cases the patients had either anaplastic or large bulky tumours.

Wertheim's Hysterectomy

In assessing the results of Wertheim's hysterectomy the effect of radiotherapy given before or after operation

TABLE X—RESULTS OF ALL TREATMENTS IN 1944–51
(437 patients seen, 421 treated)

Stage	Total seen	No. treated	5-yr. survival	Lost	Intercurrent disease	5-yr. survival-rate	Absolute survival-rate
I ..	97	97	61	1	6	62·9%	62·9%
II ..	195	192	89	1	6	46·4%	45·6%
III ..	102	101	21	0	6	20·8%	20·6%
IV ..	43	31	—	—	—	—	—
I & II	292	289	150	2	12	51·9%	51·4%
All ..	437	421	171	2	18	40·6%	39·2%

TABLE XI—RESULTS OF RADIOTHERAPY 1944–51
(334 cases)

Stage	No. treated	5-yr. survival	Lost	Intercurrent disease	5-yr. survival-rate
I	48	29	1	5	60·4%
II ..	165	79	—	5	48·5%
III ..	93	19	—	6	20·4%
IV.. ..	30	—	—	—	—
I and II ..	211	108	1	10	51·2%
All ..	334	127	1	16	38·0%

must be considered. In 1933–43, 64 of 170 patients received radiotherapy, and in 1944–57, 56 of 71 patients also received radiotherapy.

Table XIV gives the results of Wertheim's hysterectomy in 1933–51 in detail according to the type of radiotherapy given. The number of cases was too small to compare the results before and after 1944. There was a great improvement in the results where preliminary radium was used. The survival-rates of patients with stage-I and stage-II cancer for Wertheim's hysterectomy alone was 34%, but if radium were used preoperatively, the rate rose to 56%.

The primary mortality from Wertheim's hysterectomy was 15·8% in 1933–35, 5·5% in 1936–43, and 1·4% in 1944–51. 4 patients whose planned treatment was radiotherapy were subsequently treated by Wertheim's hysterectomy because of failure to respond to irradiation: 2 stage-I patients were alive and well in five years, and 1 stage-I patient and 1 stage-II patient died of cancer within that time. The lymph-nodes were free from growth in the first 2 cases, but were involved in the last 2.

TABLE XII—RESULTS OF WERTHEIM'S HYSTERECTOMY 1944–51
(71 cases)

Stage	No. treated	5-yr. survival	Lost	Intercurrent disease	5-yr. survival-rate
I	43	28	—	1	65·1%
II ..	23	9	—	—	39·1%
III ..	5	1	—	—	—
I and II ..	66	37	—	1	56·1%
All ..	71	38	—	1	53·5%

Carcinoma of Cervical Stump

In 1933–56 38 previously untreated cases of stump carcinoma were seen. The total number of new cases of carcinoma of the cervix during this period was 1405, giving an incidence of 2·7%, the incidence having risen from 1·9% before 1944 to 3·3% since that time, as shown in table XV.

Age-distribution.—The youngest patient was aged 37 and the oldest 79. The distribution was as follows:

Age (yr.)	30–39	40–49	50–59	60–69	70 or more
No. of patients ..	2	6	16	11	3

Parity.—Of the 38, 7 (18%) were nulliparous; the distribution of pregnancies was as follows:

No. of pregnancies ..	Unknown	Nil	1	2	3	4	5	6
No. of patients	2	7	9	7	6	2	2	3

Pathological Findings at Subtotal Hysterectomy.—The commonest pathological condition was fibroids, which were found in 18 cases. The recorded findings were as follows:

No. of cases	*Pathological Findings*
15	Fibroids.
1	Fibroids and metropathia hæmorrhagica.
1	Fibroids and endometriosis.
1	Fibroids and ovarian fibroma.
1	Fibroids and pyosalpinx.
4	Metrophathia hæmorrhagica.
1	Nil (functional bleeding).
1	Peritonitis.
1	Tuberculous pyosalpinx.
12	Not recorded.

4 of the 12 patients whose pathology was not recorded stated that hysterectomy for fibroids had been performed.

TABLE XIII—RESULTS OF TREATMENT OTHER THAN WERTHEIM'S HYSTERECTOMY OR RADIOTHERAPY 1944–51
(16 cases)

Stage	No. treated	5-yr. survival	Lost	Intercurrent disease	5-yr. survival-rate
I	6	4	—	—	—
II ..	6	1	1	1	—
III ..	3	1	—	—	—
IV.. ..	1	—	—	—	—
All ..	16	6	1	1	37·5%

TABLE XIV—RESULTS OF WERTHEIM'S HYSTERECTOMY 1933–51

Method	No. of cases				5-yr. cure			
	Stage				Stage			
	I	II	III	Total	I	II	III	Total
Wertheim alone ..	46	30	5	81	16	10	0	26
Radium followed by Wertheim's hysterectomy	48	29	11	88	30	13	6	49
High-voltage therapy after operation ..	6	5	3	14	5	2	1	8
Preliminary radium and high-voltage therapy after operation	9	8	1	18	5	3	0	8

Time Intervals.—The time-intervals between the hysterectomy and the diagnosis of carcinoma were as follows:

Time (yr.)	*No. of Cases*	*Time (yr.)*	*No. of Cases*
Less that 1 year	2	21–25	9
2–5	3	26–30	2
6–10	7	31–35	1
11–15	6	Unknown	2
16–20	6		

Results of Treatment.—In 1933–43 11 patients were treated: 2 in stage I by Wertheim's hysterectomy, 9 by radiotherapy. 2 patients treated by radiotherapy survived five years and were still alive after ten years. In 1944–51 18 patients were treated: 1, a stage-I case, treated by Wertheim's hysterectomy, has survived ten years; the remaining 17 were treated by radiotherapy, and 5 of these survived five years. The results are shown in table XVI.

Carcinoma of Cervix and Pregnancy

In 1933–56 6 cases of carcinoma of the cervix in association with pregnancy were recorded, and 1405 new cases were seen, giving an incidence of 0·43%. Table XVII shows details of these cases.

TABLE XV—INCIDENCE OF CARCINOMA OF CERVICAL STUMP

Period	Total patients seen	Stump carcinoma	Incidence
1933–43	596	11	1·9%
1944–56	809	27	3·3%
Total	1405	38	2·7%

Carcinoma-in-situ of Cervix

The diagnosis of carcinoma-in-situ was not in use before 1950; since then 17 cases have been recorded, more than half of them being diagnosed on pathological examination following either hysterectomy or amputation of the cervix. None of these patients has developed invasive carcinoma to date.

Conclusions

Since the inception of the Joint Clinic in 1944 the results of treatment of carcinoma of the cervix have greatly improved. The five-year survival-rate for patients treated by Wertheim's hysterectomy has risen from 40·8% for the years 1933–43 to 53·5% for 1944–51, and during the same periods the survival-rate for stage-I and stage-II cases treated by radiotherapy have risen

TABLE XVI—RESULTS OF TREATMENT OF STUMP CARCINOMA

Stage	1933–43		1944–51	
	No. treated	Alive 5 yr.	No. treated	Alive 5 yr.
I	5	0	3	3
II	4	2	8	2
III	1	0	5	1
IV	1	0	2	0
All	11	2	18	6

from 26·4% to 51·2%. The two groups cannot be directly compared, because the hysterectomy group is selected as regards stage-II cases; in spite of this the results of radiotherapy are similar.

The results of radiotherapy in stage-I cases are of interest because the overall five-year survival-rate of 60·4% is disappointingly low and shows less improvement than in the other stages: it has to be compared with the figure of 65·1% obtained by Wertheim's hysterectomy. However, for the radiotherapy group where the treatment was exclusively planned and given at the Joint Clinic, the five-year survival-rate is 69%. If all cases where death took place from intercurrent disease are excluded, the rate is 77% compared with 67% from Wertheim's hysterectomy. It therefore seems that radiotherapy is not only undoubtedly the correct treatment in inoperable cases but also usually the preferable treatment for operable cases.

TABLE XVII—CARCINOMA OF CERVIX ASSOCIATED WITH PREGNANCY 1933–56

Case no.	Year	Age (yr.)	Stage	Duration of pregnancy (weeks)	Pathology	Treatment	Result (at present)
1	1935	36	I	10	Squamous	Wertheim	Alive & well
2	1948	33	I	18	,,	,,	Died in 1 yr.
3	1948	38	I	16	,,	,,	Alive & well
4	1953	40	II	16	,,	Radiotherapy	Died in 1 yr.
5	1954	41	II	12	,,	Radiotherapy	Alive & well
6	1956	31	I	14	Anaplastic	Radiotherapy	Alive & well

From the small number of cases reviewed it also seems that the results of Wertheim's hysterectomy are greatly improved by preoperative treatment with radium.

The difference in results obtained according as to whether or not there has been full cooperation between surgeon and radiotherapist is most striking. There seems to be little doubt that, if the best results are to be obtained, this type of cooperation must be forthcoming for every case of carcinoma of the cervix.

Finally, we believe that the results obtained with radiotherapy by the joint clinic are probably as good as can be achieved by our present methods, but further improvement should be possible with still greater individualisation of technique and the increased availability of apparatus in the supervoltage or megavoltage range.

Summary

The cases of carcinoma of the cervix at the Chelsea Hospital for Women in 1933–56 are reported.

A joint consultation and treatment clinic, under the care of a surgeon of the Chelsea Hospital for Women and a radiotherapist of the Royal Marsden Hospital, was established in 1944. Since that time patients treated by radiotherapy have been transferred to the Royal Marsden Hospital. The five-year results for 1933–43 are compared with those for 1944–51 and discussed.

The cases of stump carcinoma and of carcinoma associated with pregnancy are also reviewed.

We wish to thank all those surgeons of Chelsea Hospital for Women, Lewisham, The Mayday, and other hospitals for their cooperation and encouragement in referring patients to the Joint Clinic.

Our thanks are also due to Mr. A. J. Bailey for the illustration.

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BLOOD-GROUPS OF A GREEK COMMUNITY WITH A HIGH SICKLING FREQUENCY

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THE discovery of a focus of the sickle-cell trait in the villages around Lake Copais (Choremis et al. 1951) has led to speculation as to the origin of this Greek community and the manner of the introduction into the region of the sickle-cell gene. In general the presence of this gene in a community is regarded as evidence of African ancestry; and in Sicily, one of the few other parts of Europe where it has been recognised, the blood-groups show, by the presence of a moderately high frequency of the Rh chromosome cDe, that there is almost certainly a substantial African component in the population.

We have already carried out tests for the ABO, MNS, and Rh blood-groups of over 100 persons without sickle cells from various parts of Greece (Choremis et al. 1953), and as briefly stated in an addendum to our previous paper, we have now tested a similar number from the Lake Copais area. The diagnosis of sickle-cell anæmia was in the first instance made clinically; subsequently some clinical cases were found not to be homozygous for sickling, and were in fact either cases of sickle-cell thalassæmia or sickle-cell-trait carries who were also anæmic. The classification of families and individuals given below therefore differs somewhat from the one given in that addendum. Altogether 8 cases of sickle-cell anæmia were confirmed electrophoretically, belonging to 6 families. In 5 of these families both parents were found to be heterozygous for sickling and in the 6th the only parent tested was heterozygous.

Tests were carried out on 21 members of 6 families known to include cases of sickle-cell anæmia. We also tested 108 persons not closely related to one another or to the sickle-cell-anæmia families; a great many of them consisted of married couples, and 21 (19%) were sicklers. It was somewhat difficult to know how to combine these data to give a true picture of the population as a whole. In the choosing of subjects for blood-grouping there had, however, been little if any selection on clinical grounds among married couples in general; and the sickle-cell-anæmia families, despite a rather high frequency of the B gene, did not differ much in their blood-groups from the rest of the population. Hence we concluded that we should get a fair sample of the population as a whole by combining the persons not belonging to anæmia families with the available parents (but no

TABLE I—THE A_1A_2BO BLOOD GROUPS OF GREEKS FROM AROUND LAKE COPAIS

Group	No. observed	No. expected	Frequency observed	Frequency expected	Gene frequencies
O	45	45·8	0·3782	0·3848	0·6204 (0·6361)*
A_1	39	37·8	0·3277	0·3176	0·2017 (0·2027)
A_2	10	10·3	0·0840	0·0867	0·0664 (0·0655)
B	19	18·0	0·1597	0·1510	0·1116 (0·0957)
A_1B	4	5·4	0·0336	0·0450	..
A_2B	2	1·8	0·0168	0·0148	..
Total	119	119·1	1·0000	0·9999	1·0001 (1·0000)

* In parentheses, frequencies in Greeks in general (Choremis et al. 1953).

other members) of the anæmia families. This gave a total of 119 individuals, of whom 32 (27%) were sicklers. The results of our tests on their blood-groups are given in tables I–III. The calculations were made as recommended by Mourant (1954). The frequency of sickling was found to be about 17% in the population as a whole. This estimate is probably near the truth, but, because selection may have been biased by previous clinical information, and some of the subjects may have been related, the sample tested cannot strictly be regarded as a random one.

Discussion

For none of the three blood-group systems concerned are the differences significant between Greeks in general (Choremis et al. 1953) and the population under investigation. But in the sample of the general Greek population the frequencies of the chromosomes cD^ue and cDe are found to be respectively 10 and 5%, whereas in the sample from around Lake Copais they are 15% and under 1%. The precise gradations between cDe, cD^ue, and cde, in Mediterranean and African populations need to be further investigated, by testing perfectly fresh red-cell samples with a range of different anti-D sera, and by a variety of techniques; but it cannot at present be stated categorically that the difference hitherto found is not due to technical causes. Since, however, the fully developed cDe chromosome (which is almost diagnostic of African origin) was found much more commonly in the general Greek population than around Lake Copais, the blood-group distribution can hardly be said to give any suggestion of an African genetical component in the Lake Copais population, and is against the possibility of any special local concentration of African genes in that area.

But, whatever may be the precise mechanism, sickling is appreciably protective against malaria due to *Plasmodium falciparum*, which was, until a few years ago, endemic around Lake Copais. It would thus have been possible for a single sickling individual to introduce the gene from Africa or elsewhere, and for the gene frequency to rise with every generation as a result of the slightly higher mortality of non-sicklers, until deaths from the homozygous sickle-cell anæmia condition became common and a state of balanced polymorphism was reached. The gene frequency changes to be expected during such a process have been worked out by Maynard Smith (1954), and with the abundant quantitative data which are now being collected in Africa it may soon be possible to estimate at least roughly how long it would have taken to reach the situation now found around Lake Copais.

The high frequency of sickling in Africa, and its relative proximity to Greece, make that continent the most likely source of the sickling gene in Greece, but other possibilities must be considered. It may have arisen by mutation, or have entered very early in prehistoric times in the course of a migration of Veddoids from Asia, who, according to one theory, entered Africa and introduced sickling there. If sickling entered from Africa, this is most likely to have happened during the extensive slave-trading of Roman times. At a later period it may have been brought by Turkish troops from Asia Minor, who almost certainly carried it to Thrace; it is, however, unlikely that it could thus have reached its present high frequency around Lake Copais in the time available.

TABLE II—THE MNS BLOOD-GROUPS† OF GREEKS FROM AROUND LAKE COPAIS

Phenotype	No. observed	No. expected	Frequency observed	Frequency expected	Chromosome frequencies		
MMS	26	25·7	0·2185	0·2159	MS	0·2388	(0·2334)*
MsMs	12	13·2	0·1008	0·1106	Ms	0·3326	(0·3079)
MNS	28	28·4	0·2353	0·2389	NS	0·0513	(0·1169)
MsNs	32	29·9	0·2689	0·2509	Ns	0·3772	(0·3418)
NNS	5	4·9	0·0420	0·0414			
NsNs	16	16·9	0·1345	0·1423			
Total	119	119·0	1·0000	1·0000	Total	0·9999	(1·0000)

† Tests were carried out for the Henshaw and Hunter antigens with negative results.

* In parentheses, frequencies in Greeks in general (Choremis et al. 1953).

TABLE III—THE RH BLOOD-GROUPS OF GREEKS FROM AROUND LAKE COPAIS

Phenotype	No. observed	No. expected	Frequency observed	Frequency expected	Chromosome frequencies		
CCDee	25	30·2	0·2101	0·2541	CDe	0·4919	(0·4485)*
CcDee	40	35·9	0·3361	0·3018	CD^ue	0·0123	(0·0000)
CcDEe	24	19·7	0·2017	0·1652	C^wDe	0·0252	(0·0000)
ccDEe	9	12·0	0·0756	0·1005	Cde	0·0000	(0·0197)
ccDEE	3	3·2	0·0252	0·0269	cDE	0·1639	(0·1591)
CcD^uee	1	0·9	0·0084	0·0075	cDe‡	0·0006	(0·0458)
ccDee	0	0·0	0·0000	0·0004	cD^ue	0·1462	(0·0957)
ccD^uee	8	8·1	0·0672	0·0681	cde	0·1598	(0·2312)
C^wCDee	5	3·0	0·0420	0·0254			
C^wcDee	1	1·8	0·0084	0·0155			
cddee	3	3·0	0·0252	0·0256			
C^wcDEe	0	1·0	0·0000	0·0083			
C^wC^wDee	0	0·1	0·0000	0·0006			
CCD^uee	0	0·0	0·0000	0·0002			
Total	119	118·9	0·9999	1·0001	Total	0·9999	(1·0000)

‡ Though the phenotype ccDee was not found among the "unselected" persons tested, family studies show that the chromosome cDe is present in the population, and its presence is therefore assumed in these calculations.

* In parentheses, frequencies in Greeks in general (Choremis et al. 1953).

Summary

The A_1A_2BO, MNS, and Rh blood-groups of 119 Greeks around Lake Copais have been investigated. Although sickling has a high frequency in this area, amounting to 27% in this group, the blood-group frequencies do not differ significantly from those of Greece as a whole, and, in particular, they show no evidence of an excess of genes from Africa or any other known area with much sickling.

One of us (H. L.) wishes to thank the Halley Stewart Trust for a grant enabling him to visit the Lake Copais area for the purpose of blood-grouping and hæmoglobin investigations. We also wish to thank Dr. Ada C. Kopeć for performing the calculations.

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In England Now

A Running Commentary by Peripatetic Correspondents

I am by nature an idle fellow. There is nothing I like less than hard work, and the more contented I am the less work I do. I have, however, one characteristic which distinguishes me from my idle friends and also from those with more industrious natures. It is that in stressful situations I find relief in burning the midnight oil and in accumulating vast quantities of the knowledge that eludes me during happier days. At such times all books open to me and their contents seep unnoticed into my agitated brain.

My parents despaired of me and doubted whether I would pass even the simplest examination. However, the timely destruction of the parental home by a flying bomb and the consequent disruption of family life enabled me to win a major scholarship to one of the greater public schools. There I spent my time in pursuits congenial to myself, if not to my elders, until the sudden loss of the religious faith in which I had been brought up gave me sufficient stimulus to matriculate. Later a fundamental disagreement with my father and the experience of being cut off irrevocably from my share in the family fortunes enabled me to win another scholarship, this time to a famous Oxford college.

No sooner had I arrived at the university than I fell in love in which I was promptly crossed, and this sent me easily through the first medical examination. After several unsuccessful attempts at the second I decided to get married, and the difficulties in performing this feat as a penniless undergraduate enabled me to proceed to a London hospital. Here life was so pleasant that I doubted whether I would ever qualify; but six weeks before the final examinations my wife obligingly became ill and my hospital even more obligingly diagnosed a fatal disease. This diagnosis turned out to be wrong, but not before I had qualified with exceptionally high marks in all subjects.

Now I am a registrar and my work is as peaceful as my home life. It suits me, but I would like to be a consultant as I think this would suit me even better. Unfortunately, to achieve this status I must have a higher qualification—I am awaiting a suitable catastrophe.

* * *

I had just excised a cyst from the buttock of the deputy chairman of the parks and cemeteries committee and was still caparisoned in cap, mask, gown, gloves, and white rubber bootees when I strode into the female ward for chronic dermatoses. The piano was open and prompted by an unpredictable whim, I sat down at it. There was a flutter of excitement among the patients. The parson's wife joined her hands in a kind of quiet and cosy ecstasy. "The doctor's going to play!" Those who were not confined to bed gathered round. In a bed next the piano slept a pale schoolgirl with vulgar acne. Better, I reflected, be awakened by Bach than by anyone. So I began the *First Prelude* (Book 1). I chose this piece because in twenty years of study and practice I have been able to commit only two things to memory. This was one of them. Mind you, I played it with feeling; with unusual sensitivity. *Andante*, of course. I could see that it was going down well, so before the last chord had had time to take a good grip of the strings I started *Finlandia*, which is always good for an encore. It was, in any case, my other tune. At the end there was such sincere and heart-warming applause and cries of "Encore" that I was emboldened to open the top of the piano and take off my surgical gloves. I played *Finlandia* again.

Through a receding tide of smiling and admiring females I made my way towards the door with my head slightly bent forward in an attitude that cannot be adopted with safety by any but the most profoundly modest. If there was something that unsettled me, something that may have robbed the occasion of the full sweetness of success (if indeed I was even remotely interested in *that*) it was that the acne child seemed to be still asleep. And I had opened the piano top.

I got back to the theatre flushed but happy and began the next case, which was the desiccation of a mole. It seemed fearfully terrestrial after the other-worldness of the last few minutes. I was in the middle of this job when I heard the wireless in the ward playing the *Study in C minor* (No. 12 Opus 10). This is, of course, the pianist's Parnassus. It should be attempted only by the great. As I said to nurse, "Women are simply incapable of playing this study: they have neither the wrist-power nor the emotional reserves to sustain it." As if possessed by a power higher than myself I got up from the theatre-table and walked in a kind of somnambulistic trance towards the ward door. I was not unconscious that nurse was watching me with a strange mixture of embarrassment, confusion, and unbridled admiration. She was, I suspect, uncertain. But then how could she know how deeply I was moved? The hospital secretary popped his head round the corner.

"Might be Backhaus," I said.
"Back where?" he asked.
"Or Iso Elinson."
"Is who what?"
"No Claudio Arrau. That incisive touch! I would know it anywhere . . . What magical male incisiveness! What technical supremacy . . . perhaps lacking that full-blooded passion of Elinson . . . but brilliant all the same . . ."

I opened the door so that we could all hear a little better. The acne child was seated at the piano.

* * *

In these days of relatively efficient motoring it is interesting to hear tales of earlier times. One of my patients, a very young man of 80, was lately recounting to me his early motoring exploits.

He worked for a shoe factor, and part of his duties was to deliver repaired shoes to the wilder parts of the Cumbrian fells and valleys. He started his driving career with an early model of Ford. One Friday evening, the main business of the day being finished, his employer took him over Shap Fell and in one lesson taught him to drive. The next day he was sent out on his round with the car by himself. On this first trip out he came across a steep hill at the approach to one hamlet, and the car failed to get up the hill. It failed three times and each time he had to reverse the car down the hill "and I'd never reversed a car before". After the third failure he got out to examine himself and the car. He then noticed a man standing in a field watching his misfortunes who gave him the following advice: "What tha wants to do is to turn its arse to t'ill." It worked.

Inquiry in the village revealed that the stranger who offered such sound advice was no other than the village idiot.

* * *

It always seemed to me that the least attainable and most civilised thing in the world is to live in pleasant rural surroundings and yet be within walking distance of one's work. For the past few months I have realised this dream, and even now as I walk home beside the fields and hedges I am uplifted by a sort of holiday mood. I don't know whether country doctors always feel like this, but I have an idea that it is only the toilers who go to and from their place of work twice a day who will appreciate what I mean. To see the bus go by without you and remain unperturbed, to startle a squirrel, stop to eat blackberries, or pick vivid autumn branches any day of the week, is bliss indeed. But, human nature being what it is, I remain only half content. I am beginning to miss the culture plates and cups of tea of the grimy labs in the busier parts of London.

* * *

QUEL NOËL!

The telephonic jingle bells
Keep ringing, and each ring foretells
The gut or gallstone which rebels
And hope of silent night dispels.

Hark! The herald angels sing:
"Doctor, please come quick and bring
Roller gauze, and splint, and sling;
Harry fell while carolling."

O come ye faithful, come this way
To waiting-room, you feckless fray,
To frostbite, flu, and fractures prey
From Christmas Eve to Hogmanay.

Letters to the Editor

A FUNCTIONAL NECESSITY

SIR,—This is one of the unusual occasions on which I find myself at variance with *The Lancet*, which is generally noted for its wisdom in times of professional controversy. I fear that the creation of a new subconsultant grade will only add discontented senior registrars to disgruntled S.H.M.O.s, and I am in no way influenced in its favour by the list of duties which you (Dec. 14), suggest are appropriate to a specialist rather than a consultant. These duties, you rightly say, can be done by registrars, but you go on to say that for those who do not later get consultant appointments the specialist grade should offer permanently satisfactory conditions. Surely no-one wants to be a permanent registrar, and intellectual satisfaction must be one of the conditions. Unfortunately there are three separate problems: (1) the recruitment of junior hospital staff (which is linked up with the difficulties of entry into general practice); (2) the proper employment of S.H.M.O.s; and (3) the opportunities for senior registrars who are *already fully trained* for consultant posts. It is the last of these problems which is the most urgent at the present time. It is linked with the first but not, in my view, with the second problem—at any rate in general medicine and surgery.

No-one, I think, would object to the creation of assistant physicians and surgeons where such appointments are appropriate, but they must have a right of succession to senior consultant posts which is practically automatic. It is better that a few mistakes should be made (as they are in appointments in all professions) than that morale should suffer and a new "senior-registrar problem" be created at a somewhat higher level in a few years' time.

Having taken up my pen I should like to make one or two more observations. A review of consultant appointments there must be, with, we hope, the creation of new vacancies. We are repeatedly told that more consultants are needed. If so, more of the pressure should be coming from our own profession in the places where they *are* needed. We cannot expect the Ministry to make all the moves, and then blame them for interference and central control, but a little encouragement from the Ministry to the regional boards would be a welcome sign of their desire for a satisfactory solution. While this is going on an interim solution giving security and incremental salary to time-expired senior registrars may have to be accepted. Negotiations between the Joint Consultants Committee and the Ministry are in active process at the present time.

My college is deeply concerned that an early solution shall be found and will continue to use its influence to this end, but the main negotiation is rightly done through the Joint Consultants Committee, combining as it does, medicine, surgery, and other branches of the hospital service, and representing both the Royal Colleges and the Central Consultants and Specialists Committee of the British Medical Association.

Royal College of Physicians,
London, S.W.1. ROBERT PLATT.

SIR,—After reading the letters on the senior-registrar problem, I feel that surely the point has been missed. The ultimate in requirement is security. Everyone would like to go to the top, but obviously this is not possible.

But to throw out the man who has spent 10–15 years' postgraduate work in hospitals, and force him overseas, middle-aged, and perhaps beginning to lose his energy and vitality, and certainly his illusions, is outrageous, intolerable, and inhuman. Any firm who introduced it in business would be a laughing-stock.

A grade must be found in which (*a*) security of office is guaranteed and (*b*) promotion is possible but not inevitable. And, from the look of things, it will have to be fought for.

Hove. F. V. GRIFFITHS.

FATALITY FROM TWO COMMON SURGICAL CONDITIONS IN TEACHING AND NON-TEACHING HOSPITALS

SIR,—The stimulating article by Dr. Lee and his colleagues (Oct. 19) discussed statistically the case-fatality rate from certain common surgical conditions. In the groups assessed the case-fatality from appendicitis with peritonitis was 3·3% in teaching hospitals and 6·8% ("standardised" for age 6·6%) in non-teaching hospitals. The overall case-fatality for perforated peptic ulcer was 8·3% in teaching hospitals and 11·8% in non-teaching hospitals. These figures have given rise to a certain amount of misgiving, particularly in non-teaching hospitals, and we therefore decided to investigate the case-fatality of all patients in these two clinical categories in Kingston Hospital from January, 1956, to September, 1957. All the case-notes were carefully inspected by us personally.

Table I gives the fatality-rate at Kingston Hospital in cases of appendicitis with peritonitis. To give as objective a figure as possible, only those cases were taken in which gangrene, perforation, or frank pus were noted at operation.

TABLE I—NO. OF CASES OF APPENDICITIS WITH PERITONITIS (deaths in parentheses)

Age (yr.)	Cases with gangrene and/or perforation		Other cases with frank pus in peritoneal cavity		All cases		Case-fatality (%)
	M	F	M	F	M	F	
0–15	21 (0)	12 (0)	3 (0)	3 (0)	24 (0)	15 (0)	0
15–65	41 (0)	29 (0)	12 (0)	10 (0)	53 (0)	39 (0)	0
65+	7 (1)	10 (1)	3 (0)	3 (0)	10 (1)	13 (1)	9
All ages	69 (1)	51 (1)	18 (0)	16 (0)	87 (1)	67 (1)	1
Both sexes	120 (2)		34 (0)		154 (2)		

The only deaths in our series were of a man, aged 85, who died five days postoperatively, necropsy showing extensive infarction of several days' standing, and a woman, aged 67, who died of pulmonary embolism on the ninth day.

Table II shows the case-fatality in perforated peptic ulcer at Kingston Hospital. The patients who died in this series were aged 52, 68, 71, 72, and 74. The series was investigated further by method of treatment (table III), some closed by omental graft and others by partial gastrectomy—the latter only by consultant or senior registrar.

TABLE II—NO. OF CASES OF PERFORATED PEPTIC ULCER AND NO. OF DEATHS BY AGE OF PATIENT (MALES)

Age (yr.)	Cases (and deaths)	Case-fatality (%)
0–45	10 (0)	0
45–65	35 (1)	3
65+	12 (4)	33
All ages	57 (5)	9

The case-fatality for patients of 65 and under is less than half that in the teaching-hospital group and a quarter to a third that in the non-teaching-hospital group in the General Register Office (G.R.O.) statistics. In the over-65 group, the figure is approximately the same as in the G.R.O. groups.

TABLE III—TREATMENT OF PERFORATED PEPTIC ULCER (MALES)

Age (yr.)	Treated by suture	Treated by gastrectomy	Total	Fatality (%)
0–45	6 (0)	4 (0)	10 (0)	6
45–65	26 (1)	9 (0)	35 (1)	3
65+	6 (3)	6 (1)	12 (4)	33
All cases	38 (4)	19 (1)	57 (5)	9

Kingston Hospital is an acute general hospital of 534 beds, including 118 acute general surgical beds. It serves a population of about 200,000, and it was estimated that 12% were over the age of 65 in 1951. The hospital is an old building in which modern adaptations are gradually being carried out.

The result of our investigations from actual cases certainly does not bear out the suggestion that the case-fatality rate in non-teaching hospitals is twice as high as that in teaching hospitals, so it would be helpful to have for comparison the case-fatality figures for all cases in the two clinical groups from non-teaching hospitals taking part in the G.R.O. inquiry.

It would be interesting to hear from statisticians how they can hope to get valuable information from a 1-in-10 sample from such a varied assortment of hospitals as one finds in the National Health Service. Very few hospitals are alike in the proportion of their beds allocated to the various specialties. The figures submitted from the individual hospitals will be prepared, most likely, by junior staff in the records department, and may even be compiled from medical notes which have not been carefully vetted by experienced medical staff. Figures are valuable only if medical details have been fully inserted and patients have been relegated to the proper category by doctors with experience, working on a standard basis.

We were interested to read in the letter from Mr. Barrett (Nov. 2) that the case-fatality rate was 3·03% for all cases of appendicitis with peritonitis in 1951 at Leicester Royal Infirmary. Mr. Barrett's remarks about certain missing cases support our contention that the G.R.O. figures from non-teaching hospitals should be carefully checked.

We are submitting the figures from Kingston Hospital at the request of the medical staff committee to show that the G.R.O. figures do not apply to all non-teaching hospitals, as has been implied by the lay press. The assessment of figures from individual hospitals is extremely difficult. Good results over a given period are complimentary to the hospital team, medical, nursing, medical auxiliary, and lay, in varying degree, and reflect to a large extent the quality and adequacy of the service, outlining the value of pre- and post-operative care, good anæsthesia, good surgery, good nursing, &c. Antibiotics have been largely responsible for the improvement in case-fatality figures as compared with, say, twenty years or more ago, but latterly the increase in organisms, chiefly staphylococci, resistant to our present chemotherapeutic drugs has caused an increase in postoperative sepsis with prolongation of inpatient stay. This factor, if continued, will certainly cause an increase in case-fatality rates, which may have appeared already in certain areas. Professor Platt (Nov. 2) has drawn attention to the variation in social class of patients in individual hospitals; there is in addition the availability and accessibility of general practitioners, the effectiveness of inter-district transport arrangements, and the quality and adequacy of the hospital accommodation in the area. Where hospital accommodation is inadequate, general practitioners may well tend to keep patients longer at home than they would where hospital beds were plentiful.

Kingston-upon-Thames. ALBERT A. CUNNINGHAM
LAUGHTON R. LEASK.

RESEARCH AND MENTAL DEFICIENCY

SIR,—Dr. Kirman's article (Dec. 14) is very interesting as it focuses attention on mental deficiency, but I feel that it unintentionally tends to perpetuate two misconceptions.

Firstly, the opening paragraph ends ". . . in over 70% of cases mental defect is due to genetic factors and that very little can therefore be done about it." Dr. Kirman does not appear to me to point out sufficiently strongly the error of this statement. One has only to look, as he says, at phenylketonuria and galactosæmia to realise that although we are powerless to alter the generic make-up of these patients, we can modify the clinical picture to a great extent by suitable adjustments to the environment, such as phenylalanine-low diets, &c. It seems imperative that the common misconception that all genetic diseases are untreatable should be corrected.

Secondly, one feels, on reading this article, that mental deficiency is a disease. I would point out that greater progress is likely to ensue if mental defect is considered only as a non-specific symptom of developmental failure. There are other aspects of developmental failure that can be studied more objectively than intellectual deficit, and it is only by adding up all these aspects of developmental failure that order will appear out of the heterogeneous collection of diseases that are often labelled mental defect.

Botleys Park Hospital,
Chertsey, Surrey. GORDON DUTTON.

COMPARISON OF CARDIAC AND PYLORIC SPHINCTERS

SIR,—Like Professor Johnstone (Nov. 30), we too had imagined that the pyloric sphincter is usually tightly contracted. He argues that we failed to demonstrate the tonically contracted sphincter because the pylorus was paralysed by our chain of balloons. This argument is untenable because we recorded phasic pressure waves from the pylorus (illustrated in figs. 9 and 10) whenever the antrum and duodenum showed contractions. Moreover, these balloons constitute the simplest and most reliable method known to us of demonstrating a tonically contracted sphincter where this exists, as, for example, at the cardia.

We cannot answer Professor Johnstone's queries about gastric emptying during routine barium-meal examinations in patients because we have not yet recorded the pressure-gradients across the pylorus under these conditions. Our observations on the normal pylorus were made on medical staff and students, either fasting or after a variety of familiar foodstuffs.

University College
Hospital Medical School,
London, W.C.1. M. ATKINSON
D. A. W. EDWARDS
E. N. ROWLANDS.

BRONCHOSCOPY AND TRACHEOTOMY IN FULMINATING PNEUMONIA

SIR,—We have read with interest the article by Dr. Roberts (Nov. 9) and the contrasting opinions expressed by Dr. Sheldon (Nov. 23) and Dr. Rawlins (Dec. 7).

We have, during the past two years, assisted in the treatment of several patients with fulminating staphylococcal pneumonia, and feel that the following brief case-reports support the argument in favour of bronchoscopy and/or tracheotomy in the management of this condition :

CASE 1—A girl of 18 with staphylococcal bronchopneumonia was admitted to hospital on Feb. 25, 1955. She was treated with antibiotics, 'Alevaire,' and postural drainage with some success until Feb. 27 when she developed evidence of respiratory obstruction. Laryngoscopy at this stage showed a mass of membrane in the posterior commissure of the larynx extending down into the trachea. We considered that bronchoscopy could possibly cause laryngeal œdema and increased respiratory obstruction, and went on immediately to tracheotomy. The trachea was cleared of thick mucopus, almost in the form of casts. Bronchoscopy through the tracheostomy showed gross œdema and injection of the trachea down to the bifurcation, but no further mucopus was seen. Only small quantities of sputum were aspirated via the tracheostomy tube during the next 24 hours, but the patient was comfortable and much less dyspnœic. Before tracheotomy she was very ill, but from then she made an uneventful recovery. The tracheostomy tube was removed after 6 days.

CASE 2—A man of 47 had a laparotomy on Nov. 26, 1957. On Nov. 28 he became very ill with increasing dyspnœa and cyanosis. He had generalised rales over both sides of the chest and was coughing up thick sputum, which was found to contain *Staphylococcus aureus*. In spite of treatment with antibiotics, hydrocortisone, oxygen, and 'Alevaire,' his condition deteriorated and by Nov. 29 peripheral circulatory failure developed due to the combined effect of toxæmia, extreme dyspnœa, and anoxia, and he was unable to cough

up his sputum. Bronchoscopy was performed and a large volume of sputum was aspirated from the trachea and main bronchi. There was an immediate improvement in the patient's colour and a decrease in respiratory-rate, but within 30 minutes he had relapsed to his previous state. Tracheotomy was then performed and a further large volume of sputum was aspirated.

Aspirations via the tracheostomy tube were continued as required, with dramatic improvement in the patient's general condition. He has continued to make a good recovery. The tube was removed after 10 days.

We doubt whether anyone who has witnessed the relief that bronchoscopy and tracheotomy produce in this type of case will be deterred by Dr. Roberts, who seems to be condemning a line of treatment from laboratory findings rather than from a bedside assessment of the patient.

We agree with Dr. Sheldon's dislike of repeated bronchoscopy, but for a rather different reason: should an initial bronchoscopy reveal the presence in the trachea of almost solid exudate, as in the first case described above, or should the bronchial tree fill quickly with fresh sputum soon after aspiration, then tracheotomy should be done immediately.

Pitman and Wilson [1] detailed the advantages of tracheotomy in acute respiratory embarrassment, and emphasised that the relief of respiratory obstruction in acute pulmonary disease is of paramount importance.

We are in complete agreement with this concept, but feel strongly that if tracheotomy is to be of real value in the management of these cases, it must be done in good time, and certainly not left until the patient is "black with tracheal obstruction".

Tindal General Hospital,
Aylesbury, Bucks.

J. L. ANDERSON
W. McN. NIBLOCK.

LEAD POISONING IN A DOG

SIR,—The correspondence about diabetic dogs [2 3] prompts me to write about the illness of an Alsatian pup.

He was bottle-fed on a modified cow's-milk mixture, in amounts calculated from a human-baby volume/weight formula. The mixture also contained a few drops of 'Pentavite' (a vitamin preparation). A reference giving the correct compositional formula of dogs' milk was not found until after the bottle-feeding period was over.

Despite the incorrectness of the milk composition, all went well for the first 4 weeks. This I attribute to the fact that feed volumes became considerably larger than our calculations showed they should have been. The pup did become rather bloated after feeds, but this usually passed off within an hour or so. He was also put on a meat-mince diet very early and this may have offset the milk deficiency.

When he was 5 weeks old he became extremely weak in the hind legs. The legs were not paralysed, but he could not support his weight on them. Apart from this he seemed fit and cheerful.

There were no obvious abnormal findings in his hips, but a radiograph was taken to exclude the possibility of a congenital dislocation. The films showed thick white lines just proximal to the epiphysis, and my first thought was that perhaps he had a peculiar form of scurvy. But Fairbank's *Atlas of General Affections of the Skeleton* contained no pictures of scurvy or rickets at all like the pup's films.

Next evening I heard him in his makeshift kennel (made up from an empty tea-chest), chewing away at the tinfoil lining. Another inspection of the radiograph showed pieces of foil in the lower bowel: he had lead poisoning. He also had a blue line around his gums, but as pigmentation within the mouth is common in dogs, I am not sure if this was significant.

An injection of vitamin D and colloidal calcium was given, and after 2 days he was up and about again. A week later he had an attack of abdominal colic, after he had been romping for a couple of hours (it may have been due to a temporary metabolic acidosis as a result of the exercise). This responded rapidly to another calcium injection.

Since then he has been well. The question of using sodium calciumedetate to de-lead him was considered, but no reference could be found to its oral use, so this was not done. I have since learned that an article by Boyd et al.[4] would have given me the necessary information.

General Hospital,
Launceston, Tasmania.

B. HARTLEY.

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3. Wright, J. T. *ibid.* p. 1201.

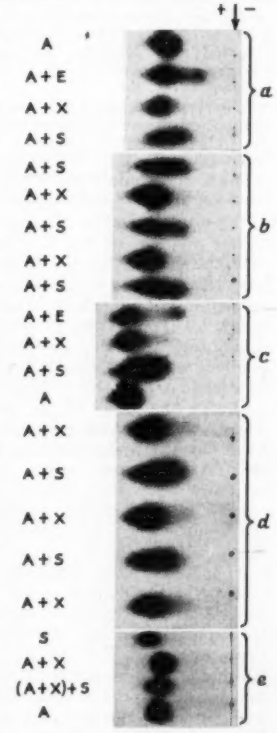
A NEW HÆMOGLOBIN IN THE BUGINESE?

SIR,—In 1956 what might be a new hæmoglobin was found among the Buginese in Sulawesi (formerly Celebes) in an incidence of about 1%. This hæmoglobin was found in the blood in addition to normal Hb A, and usually in low concentration.

At that time we reported the mobility of the hæmoglobin as slightly slower than that of Hb S but definitely faster than that of Hb E at pH 8·6. After repeated examination we found that the impression one gets of the mobility on paper electrophoresis at pH 8·6 depends on the concentration of that hæmoglobin in the solution, the mobility being higher at lower concentration. (A similar phenomenon was observed in Hb E in the homozygous condition compared with the trait.[5 6])

The impression one gets of the mobility ranges from hardly visible or just a small trail behind the A (fig. *a*) between A and S (fig. *b*), just like S (fig. *c*) and sometimes even slightly less than S (fig. *d*). As it very often seemed like S but did not give any sickling, it was thought that it might be Hb D. Compared with Hb S at pH 6·5, however, we always found a slight difference, our hæmoglobin being slightly slower (fig. *e*), so that we did not dare to publish it as Hb D, which according to the original publication of Itano [7] must have the same mobility as Hb S at pH 8·6 and pH 6·5.

After repeated study we are now still of the opinion that this hæmoglobin may be a new type of hæmoglobin.



(*a–d*) Paper electrophoresis at pH 8·6 of an unusual hæmoglobin (X) in Buginese; (*e*) the same hæmoglobin) X) at pH 6·5.

Prof. J. H. P. Jonxis, who kindly examined this hæmoglobin in the Tiselius apparatus, found that it was slightly faster than Hb S at pH 8·6 and suggested the possibility of this hæmoglobin being Hb G. But Dr. H. Lehmann, who kindly compared it with Hb G, was of the opinion that our hæmoglobin is certainly not hæmoglobin G.

This is again an illustration of how the electrophoretic method, although a marvellous advance in the field of hæmoglobin study, is not entirely satisfactory.

Department of Parasitology
and General Pathology,
University of Indonesia,
Djakarta.

LIE-INJO LUAN ENG.

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5. Lie-Injo Luan Eng. Thesis, University of Indonesia, 1956.
6. Lie-Injo Luan Eng. *Lancet*, 1957, i, 20.
7. Itano, H. A. *Proc. Nat. Acad. Sci., Wash.* 1951, 37, 775.

INFANTILE GASTROENTERITIS

SIR,—Dr. Brown and Dr. Bailey (Dec. 14) report that there are many unjustifiable admissions to gastroenteritis units. I entirely agree and wish to offer a possible explanation.

It is insufficiently realised that there are many other causes of diarrhœa and vomiting in infancy as well as infective gastroenteritis and that gastroenteritis is unlikely to be the diagnosis unless anorexia and a certain amount of toxæmia are also present. This misconception is particularly unfortunate in the underfeeding syndrome.[1–3] It is the more than usually vigorous babies who are most prone to be underfed, since an average diet is unlikely to be sufficient for them, and if their hunger is aggravated by a period of starvation, the usual treatment for gastroenteritis, their reaction may be such that the parents *give* up the struggle in desperation. My impression is that many "gastroenteritis" admissions, especially infants under 3 months old, fall into this category.

Although many different factors have to be considered in each case, and even then the diagnosis may remain conjectural, I would suggest the following general rule. If an infant with diarrhœa and vomiting refuses his feeds, but is thirsty, infective gastroenteritis is likely to be the diagnosis and a period of starvation is indicated; but if he is hungry, feeding him until his appetite is satisfied, with either half-cream or full-cream milk as thought fit, is unlikely to do harm and often effects a cure.

Ruchill Hospital,
Glasgow. H. G. EASTON.

COMBINED BARIUM MEAL AND CHOLECYSTOGRAPHY

SIR,—The article by Professor Johnstone and Dr. Sumerling (Nov. 30) interested me particularly on account of their statement that 48% of patients with a normal cholecystogram were found to have disease of the upper alimentary tract. While appreciating that they are concerned primarily with evaluating the technique of combined barium meal and cholecystography, I feel that their observations would be of particular value to surgeons if they could separate the group of "pathological gallbladders—i.e., non-functioning, or functioning with demonstrable gallstones" into its two components.

Clinically, the functioning gallbladder with gallstones presents a problem, and a particularly difficult one, which resembles that of the normal gallbladder more closely than that of the pathological gallbladder. Removal of a normal gallbladder is mistaken surgery, for not only will it fail to relieve symptoms, but also it is followed in a high proportion of cases—estimated at 30% by Ogilvie [4]—by symptoms attributable to the operation and for which, for lack of precise knowledge of their nature, the term choledochodyskinesia may be accepted.

Unfortunately the removal of a functioning gallbladder which contains gallstones is followed by similar symptoms in about the same proportion of cases. This is not surprising when one considers that such gallbladders at laparotomy and on microscopical examination often show no pathological abnormality. Their classification with pathological gallbladders on the basis of the stones which they contain is therefore one which clinically causes only confusion.

It is my practice always to ask for a barium meal in patients referred to me with a functioning gallbladder containing gallstones, and in many cases this has revealed a peptic ulcer, and sometimes a hiatus hernia, which may be the cause of the symptoms. On a few occasions I have at laparotomy found evidence of peptic ulcer which the barium meal had failed to reveal. I think it is important to know that cholecystectomy in such cases will relieve only such of the patients' symptoms as are due to gallstone colic—and that if there has been no colic the most that can be confidently claimed is that the patient is saved from future complications from the gallstones, but the incidence of a "post-cholecystectomy syndrome" will be something like 30%.

It would therefore be especially interesting if Professor Johnstone and Dr. Sumerling could say in what proportion of their cases of functioning gallbladders with gallstones they found lesions in the upper gastrointestinal tract and what these lesions were.

Edgware General Hospital,
Middlesex. FRANK FORTY.

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2. Wickes, I. G. *Brit. med. J.* 1952, ii, 1178.
3. Illingworth, R. S. The Normal Child; p. 74. London, 1953.
4. Ogilvie, H. *Ann. R. Coll. Surg. Engl.* 1957, **21**, 319.

PNEUMOCONIOTIC NEUROSIS

SIR,—Dr. Dünner and Dr. Hardy (Nov. 23) think it justifiable to regard bronchitis and emphysema as a direct result of inhaling irritant dust. They are right, but as Dr. Holt (Dec. 14) points out, there are other ætiological factors, and it is impossible to separate one from the other. And, although the incidence of bronchitis and emphysema is high in miners, this has not been found acceptable as grounds for awarding benefit by various committees which have reviewed the problem; one wonders why, the more so as tuberculosis, which also has other ætiological factors, is accepted as grounds for 100% compensation when found in association with pneumoconiosis. Furthermore, it is clear that emphysema of considerable degree, focal and otherwise, may be present without radiological change; and in another occupational disease due to dust—byssinosis—radiological change is not considered essential.

Argument along these lines can continue indefinitely; with pneumoconiosis there seems to be source for endless argument. What is required is a sensible, workable solution, and Dr. Gilson and his fellow correspondents (Dec. 7) have made two useful suggestions which should be further explored. I much prefer their second alternative—that of making provision under the National Health Insurance Scheme for adequate benefits for the disabled, irrespective of how the disablement has been caused. If the political difficulties were out of the way—and they should not be over-emphasised—this can be seen as largely a matter of administrative arrangement with an appropriate adjustment of contributions by employer and employee. On the subject of pneumoconiosis itself it would seem desirable to set up a committee—which must be fully independent—to review the position in the light of present medical knowledge and to re-examine the legislative side.

This problem has been in the past and still is too vexatious, absorbing time and mental energy which could be much better applied in the preventive field. The settling of the issue within the broad framework suggested by Dr. Gilson and his colleagues would confer a sense of freedom and relief to all concerned.

Clare Hall Hospital,
South Mimms, Barnet. NORMAN MACDONALD.

CONTROL OF HYPERPYREXIA IN CHOLERA

SIR,—An apparently paradoxical feature of the cholera syndrome is pyrexia, which is evidenced even in the early stages by a high rectal temperature and is in striking contrast to the great collapse and shock with cold clammy extremities and subnormal axillary temperature.

The pyrexia may be observed even before the administration of intravenous infusions. Rogers [1 2] recorded a high temperature in cholera patients who had had no intravenous saline. Of his European patients who had no saline solution about 77% were febrile.

After an infusion of saline every patient with cholera becomes feverish, usually with chill and rigor.[3] The necessity of taking a correct rectal temperature before the infusion is now well recognised. If saline infusions are given to a patient whose rectal temperature is more than 101°F, there is a great risk of fatal hyperpyrexial reactions; but if no infusion is given, the patient will probably die of irreversible shock.

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2. Rogers, L. Bowel Diseases in the Tropics. London, 1921.
3. Chatterjee, H. N., Chatterjee, K. K., Saha, R. K., Banerjee, R., Basu, D. K., Gupta, J. C., Ghosh, H. *Antiseptic*, 1955, **52**, 85.

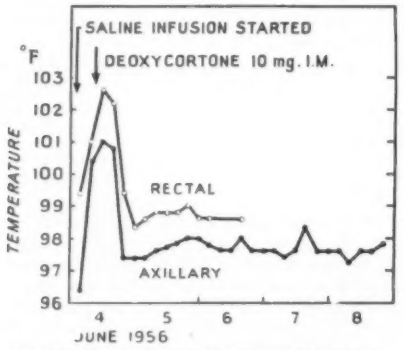

Fig 1—Temperature chart of a group-A patient.

In the epidemic of 1956 we used deoxycortone acetate (among other drugs) for treating shock, and observed that it had a remarkable action in preventing as well as combating hyperpyrexial reactions, besides maintaining the blood-pressure.

We have made a controlled study of 30 patients with an initial rectal temperature of 101°F or more, and with agglutinable cholera vibrios in the culture of stools. 26 other patients were studied but are not considered here because stool cultures were negative. Patients were allotted alternately to group A and group B.

Group A.—This consisted of 15 patients aged 10–50 years. In 12 the initial rectal temperature was between 101·2°F and 102°F; in 2 it was 103°F, and in 1 it was 104·2°F; the

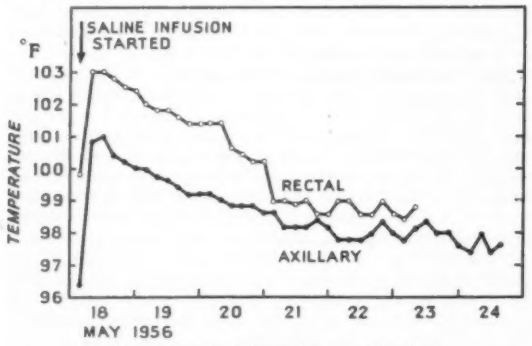

Fig. 2—Temperature chart of a group-B patient.

average temperature was 101·8°F. All the patients received deoxycortone acetate 10 mg. intramuscularly after the routine saline infusions had been started. All the patients of this group were afebrile by the end of twenty-four hours. There was 1 death due to failure of circulation.

Group B (controls).—This consisted of 15 patients aged 14–55 years. No deoxycortone acetate was given. Only 2 were afebrile after twenty-four hours. Of the remaining 13, 10 cases became afebrile in forty-eight hours. 2 died on the second day, 1 from hyperpyrexia (105°F) and failure of circulation, and the other from circulatory failure. At seventy-two hours all the surviving 13 patients were afebrile.

Both groups were given the modified treatment of cholera:

(1) For diarrhœa, coleus aromaticus [4 5];
(2) For vomiting, promethazine-8-chlorotheophyllinate ('Avomine') [5 6];
(3) For anuria, ascorbic acid and promethazine [7]; and
(4) For dehydration, saline infusions by intravenous drip after the rectal temperature had been brought to about 101°F by iced rectal saline washes, sponging, and (in 2 cases) phenicarbazidum (cryogenin).[3]

Thus it seems that deoxycortone had a definite action in controlling pyrexia and in preventing hyperpyrexia of cholera. The temperature chart of a patient from each group is shown in figs. 1 and 2.

We wish to record our thanks to Dr. P. C. Ghorai for his great help; to the authorities of Chittaranjan Hospital for their cooperation and permission to do this work; to Messrs. May & Baker, for financial assistance in paying for part of this study.

H. N. CHATTERJEE
S. K. DAS.

Chittaranjan, Calcutta.

4. Chatterjee, H. N. *Lancet*, 1953, ii, 1045.
5. Chatterjee, H. N. *Antiseptic*, 1955, **52**, 649.
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TRAINING MEDICAL STUDENTS IN PSYCHOTHERAPY

SIR,—The question of how, what, and by whom, the medical student of today should be taught is under review in many quarters. Dr. Balint's article (Nov. 23) is therefore very timely, and it is to be hoped that some of his suggestions, after discussion and modification, will be adopted.

That ever-expanding group of diseases recognised as psychosomatic are among the chief scourges of civilised life, and are, or ought to be, of great concern to the family doctor. He has the best chance of preventing these disorders by early identification of unhealthy trends in the families under his care, and, when they have developed, by providing effective treatment, and at a stage when the disease process is reversible. This all presupposes that he has the knowledge, the technique, and the time. With the understanding of psychosomatic disease as yet so incomplete it may be asked how this knowledge and technique is to be gained. But can we afford to wait before we start to teach what is already known?

I know it will be argued by some that an orthodox psychiatric approach is all that is needed to deal with psychosomatic disorders, but on this point I confess to being more than sceptical. In my experience such an approach usually fails—for instance, in colitis, migraine, and asthma. Indeed, I find that these diseases each need different psychotherapeutic techniques. For example, the avuncular, strong, protective attitude required to help colitis patients is just the one to send an asthmatic into status. In colitis there is almost always bottled-up resentment against some relative, neighbour, or friend, to be released before an attack can be cut short; in migraine and vascular headache the doctor must tackle ingrained perfectionism, inherited and imitated from an undemonstrative parent with the same high standards, and grudging in praise except for excellence. Skeletons in the cupboard there may be in this disease, but they are less common than an inability to relax in the face of increasing everyday responsibilities at home, at work, and in the community. One usually has to deal with the hovering ghost of a critical father or mother, but insight into a personality, a willingness to modify attitudes, and relaxation exercises taught by the right person, are in over half the cases immediately effective.

I have mentioned these clinical points in a sketchy way to illustrate what I mean by the need for special techniques based on an understanding of the personality traits peculiar to the disease being treated. Some will deny the existence of specific personalities, but they are in the main the least qualified to do so, as they frequently lack day-to-day experience of psychosomatic disorders.

In giving general practitioners a psychotherapeutic technique it is useless to ignore the time factor which will be constantly with them. If it is ignored they will soon become disillusioned. In this respect I can say unreservedly that knowledge of disease personalities saves time.

No-one expects a student to recognise a difficult heart-murmur the first time he hears it; he has to hear it several times. Clinical medicine is taught by example, at the bedside and in the clinic, and psychosomatic medicine should be taught likewise, and mainly by clinicians. At present too few are sufficiently orientated to undertake the task, but I am convinced that in ten years this will not be so.

Few students are mature enough before qualification to take advantage of a full course of training, and to give it will be to waste it. Teaching by example and by group discussion, as advocated by Dr. Balint, throughout the clinical years, should, however, provide an excellent introduction, and to this clinicians and all the experts in psychology should jointly contribute. I seriously recommend that the bulk of the teaching should remain for a postgraduate course about five years after qualification, possibly carrying a diploma, which should be just as essential to the majority of general practitioners of the future as obstetric recognition is today.

Ipswich. J. W. PAULLEY.

TECHNIQUE OF INTRA-ARTICULAR INJECTION

SIR,—Since the introduction of hormones of the cortisone group, intra-articular injection has been increasingly used in the treatment of arthritis. Unhappily, however, infection has followed such injections; from one clinic a case of septic arthritis has been reported, and from another, 1 fatal and 1 severe infection followed the injection of hydrocortisone. During the past fifteen years I have given, or been responsible for, on a conservative estimate, well over 100,000 injections into joints. In most of these I used a solution of lactic acid (which in addition to having the weak antiseptic action of an acid, contained a small quantity of cresol derivative as a preservative), but I have used hydrocortisone in over 500 joints.

The idea of the body as a virgin cœlom, surrounded by hosts of prowling Midianite microbes seeking entry, has been modified by the knowledge that infected foci (e.g., in the biliary and renal tracts, prostate, and colon) with associated low-grade bacteriæmia, exist without symptoms in many people, and it might be expected that such infection would occasionally be focused by the trauma of intra-articular injection; but this has not happened.

It may be of value to describe the technique I have used, since I believe it has been largely responsible for the freedom from infection. Immunity from catastrophe depends, I believe, on several factors:

(1) An *aseptic* background, and an *antiseptic* approach.

(2) Elimination of trauma by the use of needles of fine calibre.

(3) Care in the use and storage of the injected agent.

(4) An atmosphere of quiet confidence.

Asepsis and antisepsis.—Needles are boiled for at least ten minutes and stored in sterile test-tubes. No-touch technique is essential, but the flexible needle shaft is held and guided during introduction by a swab soaked in antiseptic (a weak solution of cetrimide is best). The skin is prepared with cetrimide, but scrubbing should be avoided because it may produce local hyperæmia. The injection is then made as rapidly as is consistent with care.

Needles.—For knee, shoulder, elbow, and ankle, I use a stainless-steel needle of length (2½ in.) and calibre 0·55 cm.; for the hip-joint I use needles of the same bore but of length 3¾ in.) up to 5 in. for the steatopygic. For the small joints, metacarpal or interphalangeal, hypodermic needles of size 17 are most suitable; finer sizes will not transmit the suspension of hydrocortisone. Needles of a wider bore than these, though necessary for aspiration, may cause considerable trauma to the synovial membrane, evidenced by bleeding into the joint or through the puncture. Needles are stored in phenol iodide to which is added sodium nitrite to prevent rusting. Local anæsthetic is not used.

The injected solution.—The use of a multiple-dose vial is deprecated, but it is often inevitable in a busy clinic. Where an antiseptic preservative is present there is practically no risk, but with hydrocortisone no preservative can be used. Contamination can usually be avoided by ensuring that once the needle used to withdraw the suspension has entered the vial, it is never removed; repeated removal and reinsertion has been shown to introduce organisms, particularly in an outpatient atmosphere. If any surplus fluid is left, the vial is discarded.

The atmosphere of the clinic.—I am greatly opposed to using the panoply of the operating-theatre in a joint-injection clinic. Inevitably, it gives rise to fear and expectation of severe pain; and such emotional states lower resistance.

I use a syringe of the type used for iodised oil (Burrell's) with screw-down piston, fitted with a nozzle to accept the standard "Record" needle; this is particularly useful in the hip-joint, where adhesion between the joint capsule and the femoral neck is common. The injection is made under considerable pressure, adhesions are freed, and the range of painless movement increased.

It is important to remember that entry into the capsule of the joint is the aim, and that it is unnecessary to reach the interval between the bones; for the shoulder a subcoracoid approach is best; for the elbow, laterally above the head of the radius; for the wrist, via the dorsum; for the knee, on either side of the patellar tendon. The hip-joint may need more detailed description: the needle is introduced laterally ½ in. behind the tip of the great trochanter, and directed towards the groin; occasionally also ½ in. in front of the trochanter, lest adhesions prevent the solution perfusing the whole joint. Injection over the femoral head is dangerous, for the vascular anastomosis in this region is not constant in position. This joint should be aspirated at the first injection; effusion is commoner than clinical signs indicate.

Sunderland. W. GRANT WAUGH.

CHANGING TO THE METRIC SYSTEM

SIR,—The metric system has many advantages over the imperial or avoirdupois system. It has already been adopted in experimental medicine and science, and the doses of all new drugs are rightly given in the metric decimals. It has not yet been adopted for expressing the dosage of the older drugs. What is so difficult to understand is the pusillanimous caution in the proposals for changing the system of measurement of drugs. Changed it will be—and by a bold decisive stroke it could be done overnight.

The Continent changed from an obsolete system of weight to metric units by decree from one day to the next without practical or administrative difficulty by declaring 1 kg. to be equal to 2 lb. Yet doctors and druggists in this country want five years to do what can be done in five minutes—with a little preliminary preparation. This consists merely in recalculating all doses at present expressed in grains or fractions thereof to the nearest milligramme or (when 10 or more milligrammes are involved) to the nearest centigramme or gramme, in accordance with international customary dosages. But there should be no two or three places of decimals in the interest of a spurious accuracy. One can be scientific and sensible at the same time. This could be a congenial task perhaps for some such body as the Joint Formulary Committee or the British Pharmacopœia Commission.

The act of transition should be the agreed announcement of a "zero-hour" for the change. After Jan. 1 at 12 noon, for example, doctors will prescribe and pharmacists will dispense milligrammes of drugs instead of fractions of grains—and the patients won't even know.

London, W.1. ALBERT W. BAUER.

TRIBUTE TO LORD NUFFIELD

Sir HENRY DALE and Sir CLEMENT PRICE THOMAS write:

"On Oct. 10 last, Lord Nuffield celebrated his 80th birthday. There were many then who wished to do him honour; and amongst them was a group of doctors who believed that members of their profession should have an opportunity of showing their admiration for Lord Nuffield, and their gratitude for his far-sighted generosity. They regard Lord Nuffield, indeed, as the most generous benefactor to medicine that this country has ever known, and they are convinced that there can be few medical men and women whose scientific or professional activities have not benefited, directly or indirectly, from his gifts.

"Earlier this year, therefore, this group of doctors wrote personally to many of their colleagues in this country, and caused announcements to appear in medical journals at home and in the Commonwealth for the information of others overseas, inviting contributions, however modest, towards a birthday present for Lord Nuffield, which would serve as a tribute to him from the whole profession.

"Today, Dec. 19, we as treasurers of this birthday fund, together with Dr. W. N. Pickles, had the great pleasure of lunching with Lord Nuffield in Oxford; and, on behalf of the medical profession, we presented him with a pair of diamond and pearl cuff-links and with a cheque for over £3500, in the hope that he would spend it in some way which would keep him in mind of the regard for him which it betokens.

"In paying this tribute, members of the medical profession were not unaware of the difficulty of making such a material gift to Lord Nuffield, and we were grateful to Lady Nuffield for her advice in the choice of a part of the present. In making the presentation, it was pleasant to be able to emphasise the fact that thousands of contributions had been made by medical men and women from nearly every corner of the Commonwealth, glad to be able to offer these tokens of the deep feeling of respect, affection, and admiration in which Lord Nuffield is held by the medical profession."

Medicine and the Law

Gynæcologist Wins Action Against Regional Board

A DOCTOR employed since 1937 as gynæcological surgeon and medical superintendent in a hospital owned and controlled by a local authority continued to serve the hospital after it was transferred to the regional hospital board under the National Health Service. For some months after the transfer he was mistakenly regarded by the board as a full-time officer, and he was informed by a circular letter issued by the board in May, 1949, that pending the issue of a permanent contract (which was eventually to be issued to all transferred officers) his duties as a consultant would be continued on the existing basis. The doctor, who had given up residence at the hospital to preserve his consultant status, said that he preferred a part-time contract on the basis of eight half-day sessions a week and asked to have his salary adjusted. On July 1, 1949, the board told him that his appointment and salary would be subject to the Terms and Conditions of Service for Hospital Staff agreed between the Minister of Health and representatives of the medical profession in June, 1949. The doctor continued to serve the hospital.

Early in 1950 at the request of the board a panel of doctors inquired into police allegations regarding the non-registration of births and deaths of children born prematurely at the hospital. The panel reported that the doctor's conduct in connection therewith was not culpable or deserving of censure but that he had shown a lack of tact in his attitude. Notwithstanding that report the consultant services committee of the board expressed extreme disapproval of his conduct and decided to appoint another consultant to take charge of the administrative arrangements in the gynæcological and obstetric unit of the hospital and share the beds with the doctor. A contract on a part-time basis for seven half-day sessions a week was offered to the doctor but he refused to accept the terms offered. After the offer was made he was informed that if he failed to sign the contract he would have a right of appeal to the Minister of Health under clause 16 of the Terms and Conditions of Service. He did not sign the contract but the Minister refused to entertain his appeal. He was dismissed by resolution of the board passed on Jan. 22, 1952, given three months notice, and left the board's service on April 30, 1952. He now sued the board for a declaration that he had not been validly dismissed by the board, and salary from May 1, 1952; alternatively, damages for wrongful dismissal. He also claimed that the board's decision to dismiss him was made mala fide. Against the Minister of Health he claimed a declaration that the Minister, in refusing to entertain his appeal, had acted in breach of his duty under the National Health Service Act, 1946.

Mr. JUSTICE BARRY said that the principal issue in the case—whether the doctor's employment with the board had been rightfully terminated—depended upon whether or not the contract under which he was employed incorporated the Terms and Conditions of Service for Hospital Staff issued by the Minister in June, 1949. Clause 16 of those conditions provided for an appeal to the Minister, where a consultant considered his appointment with a board to have been unfairly terminated, and on such an appeal it was the Minister's duty to obtain the advice of a professional committee and in the light of it to confirm the termination, direct reinstatement, or arrange some third solution. That procedure was to be completed before the board's decision to terminate the contract was carried into effect, and it was admitted that the appointment was terminated by the board before the procedure laid down in clause 16 had been carried out. It was clear on the evidence that the doctor was entitled to be treated as a transferred officer within the National Health Service (Transfer of Officers and Compensation) Regulations which came into effect on July 5, 1948. After the appointed day he entered into the board's employment under terms similar to those under which he had previously served the borough council and he entered into a new contract with the board as a result of their letter of July 1, 1949, which offered him continued service with the board subject to the Terms and Conditions of Service for Hospital Staffs. By continuing to serve the board after the receipt of that letter he must be deemed to have accepted the offer and his contract was henceforth regulated by the Terms and Conditions. That being so, his contractual right was that his employment should not be terminated until the machinery in clause 16 had been put into effect and a decision reached by the Minister on his appeal. Therefore the termination of his services on April 30, 1952, was a breach of the board's contractual obligations to him and it followed that he was entitled to some remedy.

In considering those remedies his Lordship said that he was not satisfied that any of the persons concerned had acted in bad faith or intended to act in bad faith but had acted in what they believed to be the best interests of the hospital. The doctor was not entitled to a declaration that his dismissal was invalid. His contract with the board was in essence an ordinary one between master and servant and therefore his only remedy was damages. Had the matter gone before a professional committee as provided by the Terms and Conditions of Service the committee would almost certainly have advised the Minister that a very substantial element of unfairness had entered into the dismissal. The Minister would have acted on that advice and the doctor would have been kept on at the hospital. A fair period for the recovery of his salary was five years, to which should be added the loss to his private practice entailed by the exclusion of his private patients from all the hospitals in the board's area. Making allowance for income tax his Lordship awarded the doctor damages of £7437 10s. against the board and made a declaration that the Minister had acted wrongly and in breach of his duty under the National Health Service Act, 1946, in failing to hear the appeal. He gave judgment for the doctor accordingly.

BARBER *v.* MANCHESTER REGIONAL HOSPITAL BOARD AND ANOTHER. *Queen's Bench Division*: Barry, *J.* Dec. 13, 1957. Counsel and solicitors.—J. Scott Henderson, Q.C., and A. C. Munro-Kerr (Ponsonbys); John Foster, Q.C., J. T. Molony, Q.C., and Alan Garfitt (Solicitor, Ministry of Health, for Solicitor, Manchester Regional Hospital Board).

E. M. WELLWOOD,
Barrister-at-Law.

Action for Slander

AN action for slander brought by a county medical officer of health against a member of the county council was tried by Mr. Justice Hinchcliffe at Staffordshire Assizes on Dec. 9.

The plaintiff was Dr. Gerald Ramage, of Rowley Avenue, Stafford, and the defendant Alderman George Wilfred Newman, of Brereton, near Rugeley, an industrial social-welfare organiser and a member of the Staffordshire County Council.

It was alleged that at a meeting of the Staffordshire County Education Committee on April 6, 1957, the defendant, in the presence of a number of people, said of the plaintiff: " He is cleverer than you think. I have known him longer than you. There is a limit as to how far you can trust him." It was stated that the words complained of were spoken at the end of a meeting during which the defendant had criticised the wording of certain forms sent to parents whose children, it was considered, should go to county special schools.

On behalf of the plaintiff, it was contended that the words meant that he was false, unscrupulous, and untrustworthy in his behaviour as medical officer, and that he was therefore unfit for that position. The defendant denied speaking the words complained of, and said further that the words did not mean what was alleged, and that they were incapable of any of the meanings alleged or of any defamatory meaning.

In giving judgment, Mr. Justice Hinchcliffe said that he could not believe that five witnesses called by the plaintiff had " come to mislead the court ". All that the defence witnesses had been able to say was that they did not remember that the words were used. He found that the defendant did speak the words complained of, and in his opinion the words were defamatory in the ordinary and natural meaning. Awarding the plaintiff 150 guineas damages, and costs, the judge remarked that it was a sum " to make it clear that slanderous and offensive statements are not to be tolerated ". After the case Dr. Ramage stated through his solicitor that the damages would be given to the N.S.P.C.C.

Messrs. Le Brasseur and Oakley, solicitors instructed by the Medical Protection Society Ltd., acted for Dr. Ramage.

Obituary

LIONEL EVERARD NAPIER

C.I.E., F.R.C.P.

THE name of L. E. Napier will always be associated with the important disease—kala-azar—to whose study he devoted the greater part of his career in India and on which he was the acknowledged authority. But he was much besides a specialised investigator, and in his last years he made for himself a new place in London medicine. His death on Dec. 15 will be regretted by many colleagues who appreciated his critical ability, his experience, his unobtrusive courage, and his agreeably astringent humour.

He was born in 1888, the son of the Rev. J. Russell Napier, vicar of Old Windsor. From St. John's School, Leatherhead, he went to St. Bartholomew's Hospital and qualified in 1914. After holding house-appointments he joined the R.A.M.C. in 1915 and served as pathological specialist in India and Mesopotamia. At the end of the war he came back to England; but he was persuaded to return to India by Robert Knowles, who had been appointed to a chair at the reorganised School of Tropical Medicine in Calcutta. His post was that of research-worker in the school, but he soon made his mark also as a clinician. He worked in full collaboration with Knowles, and together they showed for the first time that *Leishmania donovani*, the causal organism of kala-azar, develops into flagellates in the sandfly, *Phlebotomus argentipes*. This initiated the intensive investigation of the role of this insect in the epidemiology of kala-azar in Assam and Bengal, and in that work Napier played a leading part in Bengal. His handbook on kala-azar, written with Ernest Muir, first appeared in 1923. But his interests were wide, and he was well-read on many subjects. Having joined the staff of the *Indian Medical Gazette* in 1928, he was its editor from 1933 to 1942; and the journal—by far the most widely read in India—attained a standard of sustained excellence in advance of anything in its former history. Such was his capacity for hard work, however, that the arduous and continuous application demanded by this task did not prevent his taking a large part in all the activities of the Calcutta School—not the least being his close interest in the clinical side of its hospital for tropical diseases. In 1935 he became professor of tropical medicine and director of the school. In this position he proved a success, and he developed a style of teaching all his own. He was direct, forcible, and accurate.

Napier spent the first part of the second world war in Calcutta at his post, but in 1943 he was invited to teach in Columbia University, New York, and was also appointed visiting lecturer in tropical medicine to Tulane University (New Orleans) and to Harvard. There, towards the end of the war, he made good use of the library facilities at his disposal to write an excellent book—the *Principles and Practice of Tropical Medicine* (1946), a manual which can still be read with profit. Always interested in hæmatology, he had previously produced a useful work on *Hæmatological Technique*.

Early in 1946 he returned from America and took the appointments of specialist in tropical diseases to the Ministry of Pensions and consultant to Queen Mary's Hospital in Roehampton. These posts gave him a foothold in London which he enlarged in several directions. For many years he was sectional editor of the *Tropical Diseases Bulletin* and contributed most of the reviews on his favourite subject. He was an active fellow of the Royal Society of Tropical Medicine and he came to take a leading part in its discussions. In 1947 he took on the editorship of the *Journal of Tropical Medicine and Hygiene*, which he held until 1952. In 1951 he relinquished his post at the Ministry of Pensions, and until last year he devoted most of his energies to the new medical dictionary being prepared for the Caxton Press. In his home at Silchester, named after the Napier family's great house in Edinburgh, he applied his taste and talent and drive to the creation of a large garden which was a joy to visiting children (as well as adults) because it abounded in geese and chickens and dogs and cats. He and his wife, Ella, had two grandchildren, the children of his son, John, who is reader in anatomy at the Royal Free Hospital.

Slightly detached in manner, though sometimes downright in opinion, Napier was consistently helpful and a most valuable friend. He will be remembered not only for his work but especially as a person, as is shown by these two tributes:

I shall always think of Leo Napier as an intensely human man of simple tastes, whose quiet friendly front concealed a keen critical mind capable of prodigious effort. He was modest and self-critical about the importance of his very considerable contributions to parasitology and tropical medicine. Indeed, it was hard to get him to talk about his own work, but when he did so he drew from a tremendous fund of personal knowledge and experience. He did not enjoy talking technical jargon. He was at his best chatting about ordinary things, especially about words. The latter had a special fascination for him which I think explained his last venture, the production of a long-needed up-to-date medical dictionary. I hope this task was finished, or near

enough to finished, because I can think of no-one who could have done it better.

I knew Napier well in the last few years, especially as a co-examiner. Personality comes out in examining, and I often listened with great respect to the kindly searching way in which he could make a candidate feel at ease and give of his best. He was generous in his assessment of candidates, as indeed he was of everybody, but he had no time for fools.

His place in medicine is assured, as a scientist skilled in the laboratory and field study of Indian endemic diseases, and as a clinician and teacher, especially in his apogee, as director of the Calcutta School, where his name is a sturdy legend. But I think his immediate memorial may well be his remarkable textbook (he preferred to call it a reference book) on tropical medicine, a large volume of erudite information and clear exposition covering the whole subject and written, every word of it, by Napier himself in an incredibly short time during the war.

I remember him as a friend. I was personally and professionally much the richer for knowing him.

B. G. M.

Napier had an original mind, suited to research and inquiry, and his record of research in kala-azar, malaria, and the anæmias will ensure for him a distinctive place in the history of the development of knowledge of diseases of hot climates. But he also had an unusual sense of literary values and of the meaning of words. To the immense and laborious work of editing a medical dictionary he brought all his gifts of penetrating scholarship and wide knowledge.

Even in dictionary-making his sardonic sense of fun asserted itself; he had in his make-up a satirical streak which made him an amusing and entertaining companion, perhaps most evident in the congenial company of the Royal College of Physicians dinners, or at the Royal Society of Tropical Medicine and Hygiene. His satire was allied to a certain combative tendency and a liking for controversy which were sometimes misunderstood. But he was generous and attractive, and those who knew him well, as I did, developed an affection for him which I find it hard to express fully in words.

C. W.

MAURICE MITMAN

M.D. Lond., F.R.C.P., D.P.H., D.M.R.E.

As we announced last week, Dr. Mitman, consultant physician and medical superintendent of Dartford River Hospitals, died at Joyce Green on Dec. 13 after a long illness.

He studied medicine at Guy's Hospital and had been junior assistant bacteriologist there for a year when he qualified in 1923. After holding house-appointments at Guy's he became assistant medical officer (and later deputy medical superintendent) at St. Marylebone Hospital, and in 1926 he took the degree of M.B. with honours. He also held a clinical assistantship at the St. John's Hospital for Diseases of the Skin, and in 1928 he was awarded the Chesterfield medal of the London School of Dermatology.

In 1930 he took the D.P.H. and D.M.R.E., and soon afterwards he joined the London infectious hospitals service while it was still under the Metropolitan Asylums Board. On the transfer of the service to the London County Council, Mitman became a divisional medical officer in the public-health department. When a vacancy arose he was appointed medical superintendent of the Eastern Hospital (L.C.C.) and later, much against his wishes, was translated to Joyce Green Hospital. In 1945 he was elected F.R.C.P. and was awarded a Dutch decoration for his work for Dutch naval casualties during the late war. He was president of the section of epidemiology and preventive medicine of the Royal Society of Medicine in 1955, and the following year vice-president of the Medical Officers of Schools Association. He was also a member of council of the Society of Medical Officers of Health. He was part-author of *Clinical Practice in Infectious Diseases*, which is now in its fourth edition.

E. H. R. H. writes:

Dr. Mitman's death is a tragedy of ill health initiated by frustration and anxiety. A clinician and administrator of outstanding ability, he converted an empty smallpox hospital into a first-rate general hospital which, during the late war, admitted civil and Service casualties. The upheaval caused by the change of authority from L.C.C. to N.H.S. in 1948 threw a strain on him, and in a letter he complained that "my new masters have created stresses which have reacted unfavourably on my health and my work".

Mitman's hobby was the collection of old glass. A good teacher and a wise counsellor, he will be sorely missed by his many friends.

Parliament

Pneumoconiosis and Byssinosis Benefit Scheme

On Dec. 16 this scheme was approved by the House of Commons. It amends the provisions of the 1952 scheme by reducing the period of qualifying employment in any prescribed occupation from twenty to ten years. This change will bring the scheme into line with the condition laid down for industrial injuries benefits. The scheme also provides for certificates of disablement to be issued by the medical board instead of by a single member of the board, thus reverting to the practice current before the 1954 amendment.

Health of Office Workers

On Dec. 19 Mr. Victor Yates introduced the Offices Regulation Bill which seeks to provide statutory minimum standards of conditions of employment for those who work in offices. It is intended to implement the recommendations of the Gowers Committee. The Bill is down for a second reading on Jan. 24 and it is third in the list.

QUESTION TIME

Regional Cost of Consultants

In 1956–57 the average cost of consultants' salaries per staffed beds of all types under the 14 regional hospital boards was as follows:

Regional board	Average cost
	£
Newcastle-on-Tyne	41·5
Leeds	28·4
Sheffield	33·6
East Anglian	36·5
N.W. Metropolitan	45·8
N.E. Metropolitan	40·4
S.E. Metropolitan	43·6
S.W. Metropolitan	30.3
Oxford	36·9
South Western	30·3
Wales	33·2
Birmingham	34·9
Manchester	28·5
Liverpool	33·6

Hearing-aids

Field trials of a transistor aid were held by the Ministry of Health earlier this year and improvements of the prototype model have since been made. This aid will be issued in the first place to children, and a first contract has been signed.

Cost of Prescriptions

The average cost of each prescription dispensed in the National Health Service was approximately 5*s*. 8*d*. in September, 1957, compared with 5*s*. in September, 1956.

Whitley Awards

On Dec. 16 the Health Ministers approved Whitley agreements relating to physiotherapists, occupational therapists, remedial gymnasts, and speech therapists.

Public Health

Clean Air Explained

LOCAL authorities have a duty to provide information to any householder within a newly designated smokeless zone, and *Family Doctor* has published a pamphlet [1] by Sir Allen Daley, Mr. Roger Smithells, and others, to meet this need. It briefly gives a great deal of information about the causes and effects of air pollution and on how to keep warm without producing more than a minimum of smoke. It has useful information about the cost and efficiency of fuels and appliances, and finds room to mention fireguards and to advocate compost-heaps instead of bonfires.

The Forward March in Mauritius

NOWADAYS it is commonplace for medical officers of health to report new low records in, for example, the infant and maternal mortality-rates; but few can report such spectacular falls as Dr. R. Lavoipierre, director of medical services in Mauritius. Between 1946 and 1955 the general death-rate fell from 29·5 to 12·9 per 1000, the infant-mortality rate from 145·2 to 67·2 per 1000 live births, the maternal-mortality rate from 10·39 to 1·47 per 1000 births, and the tuberculosis death-rate from 46 to 24 per 100,000. Much of the improvement has been due to the great fall in the number of deaths from infective and parasitic diseases (from 9·1 per 1000 in 1946 to 0·6 in 1955). *Aedes ægypti* has been eliminated, and malaria (almost) with it; Dr. Lavoipierre's report shows a photograph of a house built on what used to be a swamp. In ten years the number of cases of enteric fever has fallen by about nine-tenths.

But Mauritius has its troubles: mortality-rates, especially from tuberculosis, are still high, and spinal tuberculosis is common, though B.C.G. vaccination was started in 1951; addiction to gandia (cannabis) is increasing (or at least comes to light more often); and violence is a common cause of admission to hospital. As in European countries, the death-rates from cancer and cardiovascular disease tend to rise; and dental caries, a prime cause of melancholy among our school medical officers, is unhappily common in Mauritian school-children.

1. Clean Air: What You Can Do, What You Must Do. Pp. 32. Available to local authorities and medical officers of health from *Family Doctor*, B.M.A. House, Tavistock Square, London, W.C.1, at 2*s.* a dozen.

Appointments

FIDDLER, G. S., M.B. Edin., D.P.M.: assistant psychiatrist (S.H.M.O.), North Wales Hospital for Nervous Disorders, Denbigh.

HOSKINS, E. O. L., M.B. Edin., M.R.C.P.E., D.M.R.D.: consultant radiologist, West Wales H.M.C. group.

ROITH, EVA, M.B. Dubl., D.P.H.: M.O. for mental health, Nottinghamshire.

SEARLE, GWENLLIAN, M.R.C.S., D.O.; ophthalmologist, children's refraction clinics, Ongar and Epping.

WHITE, CLEON, M.B. Birm.: assistant M.O., West Midlands Gas Board.

Colonial Appointments:

ABDURAHMAN, A., M.B., B.SC. Glasg.: M.O., British Guiana.

BURGESS, H. J. L., M.B. St. And.: M.O., Uganda.

ESLICK, M. A. R., M.B. Lpool: M.O., South Pacific Health Service, Fiji.

FOURNIER, M. N.: M.O., Eastern Nigeria.

GHANEKAR, P. B., M.D. Bombay: M.O., Eastern Nigeria.

GOWEN, M. J., M.B.: M.O., Uganda.

INNIS, C. O., M.B. Punjab: M.O., North Borneo.

MCLAREN, D. S., M.D. Edin., D.T.M.& H.: medical research officer (grade II), East Africa High Commission.

PARKLIKOWSKI, A., M.D. Stettin: M.O., Eastern Nigeria.

PERKINS, J. D. B., L.M.S.S.A.: M.O., Northern Nigeria.

WEIR, J. T., L.R.C.P.E.: M.O., Northern Nigeria.

Notes and News

OLD PEOPLE IN MALTA

NEARLY a year ago we summarised the report [1] of the commission on medical services in Malta. Last May and June, at the invitation of Mr. Dom Mintoff, the Prime Minister, a survey of old age in the islands was made by Dr. G. F. Adams, physician to the geriatric unit of Belfast City Hospital, and Miss S. V. Cooke, head almoner at the hospital.

It was confined to people aged 60 and over—about 10% of the population—of whom, as in Britain, over 95% live in private dwellings. Social isolation seems uncommon, because of close family contacts and overcrowding and the popularity of Church activities (many old people attend twice daily). The main needs for those living at home seem to be better housing, bigger retirement pensions, and a system of domestic help.

Whereas in the "acute" hospital, St. Luke's, more than half the old patients seemed likely to go home eventually, in the long-stay hospitals all patients emphatically denied the possibility of going home. About 6% of the long-stay patients would probably have responded to reablement in a geriatric unit had there been one, but about 33% were bedfast invalids needing permanent hospital care. The proportion with contractures was about the same as in institutions in Northern Ireland, while the proportion with bedsores was lower. The incontinent and confused patients should be segregated from the others by partitions in the wards.

The Maltese start with some inherent advantages, including a short winter, innate cleanliness and gregariousness, and good nutrition. Their deep attachment to their Church provides social activity and leads to a placid acceptance of change which helps them to settle quickly into an institution (though this acceptance may prove a handicap to those who might be encouraged to return to activity if housing were provided). Dr. Adams and Miss Cooke feel that the outstanding social need is housing; if this were adequate the younger Maltese would be ready as their forebears to look after their elders. A geriatric unit should be established at St. Luke's Hospital (rather than at the long-stay hospital as suggested in a previous report) with an experienced geriatric physician, a house-physician, a State-registered nursing sister, a secretary, and (most urgent) an almoner. This unit should shift the emphasis from passive acceptance of chronic incapacity to active treatment and reablement. The number of chronic invalids would probably then be reduced, and the present long-stay hospitals would be big enough. 550 beds are needed for people who are a welfare rather than a hospital responsibility, but these could be provided at the long-stay and leprosy hospitals if the few leprosy patients were transferred. Effective social services would probably reduce the need for welfare accommodation. New building would be better devoted to housing than to new hospitals; and there should be special provision for old people in new housing schemes.

AGEING EMPLOYEES IN FURNITURE FACTORIES

TODAY increasing mechanisation in industry coincides with an increasing proportion of older men in the working community, and Mr. F. Le Gros Clark's "studies of ageing within the conditions of modern industry" now include an investigation of furniture-making [2]—mostly in the larger mechanised factories.

The industrial and medical records were examined of 251 men aged 55–76. Some working adjustments or concessions had to be made for about a tenth of those aged 55–59, three-tenths of those aged 60–64, six-tenths of those aged 65–69, and nearly all those aged 70–76. The reason for this was as often "old age" as sickness. The pace at which work is done is important; it is high with mechanisation, because much time has been used up in design, setting of machines, and reorganisation, and less can be allowed for pauses when production is underway. Coordinated timing is decisive in modern industry, and the older man tends to be too slow. On the other hand, older men are often specially suitable for repair and maintenance work, though some factories prefer to use repair-shops

1. See *Lancet*, 1957, i, 468.
2. Le Gros Clark, F. Ageing on the Factory Floor: The Production of Domestic Furniture. Pp. 36. Copies may be obtained, free, from the Nuffield Foundation, Nuffield Lodge, Regent's Park, London, N.W.1.

for training apprentices, and men who have been trained only as machinists in earlier years are unlikely to be fitted for this work. Increasing specialisation means that fewer men will be able to transfer to the repair shops, or to work on decorative and finishing processes.

LECTURES ON TAPE

PERHAPS surprisingly, it has been found [1] that students absorb from lectures more information than from reading, and nearly as much as from discussion-groups. It is, then, all the more a pity that many doctors, especially those living in the country, cannot find time or opportunity to attend post-graduate lectures. The use of tape recorders to overcome this difficulty has been proposed by Dr. J. C. Graves and Dr. Valerie Graves.[2] They suggest that the family doctor, listening to people all day, may absorb spoken information better than written; and tape has not, as has paper, "a way of accumulating like driven leaves in the doctor's house". With some ingenuity heart-sounds could be reproduced, and necessary figures could be included in booklets like those supplied by the B.B.C. to accompany school broadcasts. Discussion and special lectures could be recorded. Graves and Graves discuss the possible organisation of a central library of tape-recordings and a collection of machines for hire.

TRANSACTIONS OF THE SOUTH AFRICAN COLLEGE

IN August last year the inaugural ceremony was held of the College of Physicians, Surgeons, and Gynæcologists of South Africa, and the first issue (September, 1957) of the college's *Transactions* [3] describes the ceremony at which Sir Walter Mercer, then president of the Royal College of Surgeons of Edinburgh, was admitted to the honorary fellowship. An account is given of the events leading to the foundation of the college, and Prof. Guy Elliott, the president, refers to continuing discussions about its title. Examinations have been held this year for the fellowship of each section of the college and for the diploma in obstetrics, intended for family doctors. The *Transactions* are edited by Mr. A. J. Helfet, F.R.C.S., of Cape Town.

RHEUMATISM: BOOKLETS FOR PATIENTS

THE Empire Rheumatism Council, 8, Charing Cross Road, London, W.C.2, has issued new impressions of its booklets, one on osteoarthritis and one on rheumatoid arthritis, which doctors may obtain free for distribution to patients. Each provides useful information and advice in simple and on the whole reassuring terms. Both are amusingly illustrated by Leslie Starke.

CONNECTORS FOR BREATHING ATTACHMENTS

THE sizes of breathing attachments for connecting patients to anæsthetic machines are so many as to cause inconvenience, and even possibly to endanger the patient in an emergency. The British Standards Institution therefore recommends that two sizes of fitting should be standardised throughout the country—one for adults and one for children.[4] The object is to promote interchangeability of fitting but not to standardise design.

WHITAKER'S ALMANACK 1958

AN interesting addition to the new *Whitaker's Almanack* (1958)[5] is a comparison of the consumer goods manufactured in this country for the home market in 1955 and in 1956. The amounts decreased rapidly from 1955 to 1956. Of 35 items listed, comprising domestic furniture and equipment and motor vehicles, only 5 showed a significant increase—kitchen tables, divans, children's cots, electric blankets, and dry shavers. Other interesting new items are a table of average weekly domestic expenditure on food in 1955 at various income levels (from the annual report of the National Food Survey for 1957); a list of Government shares in public companies; statistics of independent schools; the main provisions of the Rent Act, 1957; airmail rates for parcels dispatched overseas; fire losses in 1955 and 1956 in U.K. and U.S.A.; and a table of moneys of all nations. The International Geophysical Year is described in the annual review of science.

1. Joyce, C. R. B., Wetherall, M. *Lancet*, Aug. 31, 1957, p. 402.
2. Graves, J. C., Graves, V. *Research Newsletter*, College of General Practitioners, 1957, **4**, 325.
3. Transactions of the College of Physicians of South Africa, College of Surgeons of South Africa, College of Obstetricians and Gynæcologists of South Africa. Published by the college, P.O. Box 120, Cape Town.
4. Draft British Standard for Connectors for Breathing Attachments for Anæsthetic Apparatus. CX (SGC) 8549.
5. London: Whitaker. Pp. 1190. 18*s*. 6*d*.

University of Oxford

On Dec. 14 the following degrees were conferred:

D.M.—F. J. C. Roe.

B.M.—D. I. Aitken, W. J. Harrison, M. B. Macaulay, E. H. Porter, P. G. Johnson, S. J. S. Rippon, D. R. Firth, E. S. Mucklow, Philip James, J. T. Rankin, M. J. Tarsh, A. D. Lower, C. J. Lewthwaite, P. E. Moffitt, H. V. Parry, G. R. K. Wright, M. B. Bown, J. M. Wilson, M. H. Parsons, D. H. C. Surridge, J. G. R. Flint, Donald O'Sullivan, Margaret R. Matthews, Edith M. Varley, Joan D. Peacock, D. R. London (in absentia).

University of Durham

On Dec. 14 the degrees of M.B., B.S. were conferred on the following:

T. N. Allison, Richard Carter, I. A. Crowther, Indrajeet Deepan, Eyo Ita Esua, W. A. Reay, Ruth H. Rishworth, Lilla Robinson, Vijaykumar Gokaldas Rughani, Shirley J. Rushton.

University of Leeds

Mr. C. C. D. Chandler has been appointed lecturer in the department of anæsthetics.

University of Edinburgh

Dr. Richard Scott, senior lecturer and director of the general-practice teaching unit, has been admitted to the status of reader.

Royal College of Physicians of Edinburgh

Dr. A. Rae Gilchrist has been elected president of the college. The other office-bearers for the coming year are:

Vice-president, Dr. J. D. S. Cameron; other members of the council, Dr. I. G. W. Hill, Dr. J. G. M. Hamilton, Dr. J. Halliday Croom, Dr. T. Anderson, and Dr. J. Laurie; treasurer, Dr. J. Alastair Bruce; secretary and registrar, Dr. Henry Matthew; and hon. librarian, Dr. John Ritchie.

Influenza Vaccine

Glaxo Laboratories, Ltd., announce that their Asian influenza vaccine is now generally available to the medical profession.

New Chair of Rheumatology

The Empire Rheumatism Council has endowed a chair of rheumatology which the senate of the University of London is instituting at the Postgraduate Medical School at Hammersmith. The council have already endowed a chair at Manchester University.

Increases in National Insurance Benefits

Under the National Insurance (No. 2) Act, 1957, maternity benefits will be increased from Feb. 3 and sickness benefits from Feb. 6. The new rates are:

Maternity Benefit.—Maternity grant, £12 10*s*.; home confinement grant, £5; maternity allowance, 50*s*.

Sickness Benefit.—Men, single women and widows, aged 18 and over, 50*s*.; married women aged 18 and over, 34*s*.; boys and girls under 18, 28*s*. 6*d*.

Institute of Diseases of the Chest, London

Clinical demonstrations will be arranged by Dr. F. H. Scadding at the institute (in the grounds of the Brompton Hospital, Fulham Road, S.W.3) on Fridays from Jan. 3 to March 21. Open lectures by Dr. Howard Nicholson, Dr. N. S. Plummer, Sir Russell Brock, Dr. I. Longmuir, Dr. Paul Wood, Mr. W. P. Cleland, Dr. W. H. Hudson, Mr. T. Holmes Sellors, Dr. J. L. Livingstone, Dr. Neville Oswald, and Mr. E. F. Chin will be given on Wednesdays, from Jan. 8 to March 19. All the meetings will be held at 5 P.M. and will be open to doctors without fee.

CORRIGENDUM: *Uncommon Myocardial Diseases.*—In fig. 5 of Dr. Brigden's article of Dec. 14 "fibrositis" should have been "fibrosis".

In fig. 11 (Dec. 21) the name Turner-Warwick appeared incorrectly.

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Academic and Educational

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(Queen-square)
UNIVERSITY OF LONDON
(BRITISH POSTGRADUATE MEDICAL FEDERATION)

2 COURSES OF CLINICAL DEMONSTRATIONS open to post-graduates will be held at the National Hospital, Queen-square, on WEDNESDAYS at 4.15 P.M., from 8TH JANUARY to 19TH MARCH, 1958, inclusive, and on SATURDAYS at 10.30 A.M. from 11TH JANUARY to 22ND MARCH, 1958, inclusive.

The fee for attending either of these courses is 2 guineas.

Application for a ticket should be made to The Dean, Institute of Neurology (Queen-square), The National Hospital, Queen-square, W.C.1, with a remittance to cover the fee enclosed. Only postal applications will be considered.

INSTITUTE OF NEUROLOGY
(Queen-square)
UNIVERSITY OF LONDON
(BRITISH POSTGRADUATE MEDICAL FEDERATION)

A COURSE OF LECTURES on "Neurological Aspects of General Medical Conditions" will be given in the Lecture Theatre at The National Hospital, Queen-square, London, W.C.1, on MONDAYS at 5.30 P.M. on the following dates :—

6th Jan.	Carcinoma and the Nervous System	Dr. R. A. HENSON
13th Jan.	Pituitary, Adrenal and Renal Disorders	Dr. R. E. KELLY
20th Jan.	Thyroid and Parathyroid Disorders	Dr. P. K. ROBINSON
27th Jan.	Hyperglycæmia, Hypoglycæmia, and Hyperpyrexia	Dr. DENIS WILLIAMS
3rd Feb.	Anoxia, Acapnœa, Hydration and Dehydration	Dr. JOHN MARSHALL
10th Feb.	Liver Diseases	Dr. B. G. PARSONS-SMITH
17th Feb.	Toxic Action of Metals and Organic Compounds	Dr. J. W. ALDREN TURNER
24th Feb.	Diseases due to Tissue Reaction	Dr. HELEN DIMSDALE
3rd March	Collagen Vascular Disease	Dr. HELEN DIMSDALE
10th March	Nutritional Disorders	Dr. REDVERS IRONSIDE
17th March	Vascular Degenerations	Sir CHARLES SYMONDS

The fee for the full course will be 3 guineas, or for a single lecture 7s. 6d.

Tickets may be obtained on application to the Dean, Institute of Neurology (Queen-square), The National Hospital, Queen-square, London, W.C.1.

INSTITUTE OF ORTHOPÆDICS

PROVISIONAL PROGRAMME

A COURSE OF LECTURES on "Disorders of the Spine" will be given in the Lecture Room at the Institute of Orthopædics, Royal National Orthopædic Hospital, 234, Great Portland-street, London, W.1, on FRIDAYS at 6 P.M. on the following dates :—

17th Jan.	Scoliosis I	Mr. J. I. P. JAMES
31st Jan.	Scoliosis II	Mr. J. I. P. JAMES
7th Feb.	Spondylolisthesis	Mr. P. H. NEWMAN
14th Feb.	Ankylosing Spondylitis	Mr. D. TREVOR
21st Feb.	Infections of the Spine other than Tuberculosis	Mr. C. W. MANNING
28th Feb.	Disc Lesions	Mr. P. H. NEWMAN
7th March	Osteoporosis of the Spine	Dr. R. NASSIM
14th March	Tumours of the Spine	Mr. H. J. BURROWS
21st March	Pott's Disease	Mr. J. A. CHOLMELEY
28th March	Pott's Paraplegia	Mr. H. J. SEDDON

The fee for the full course will be 3 guineas, or for a single lecture 7s. 6d.

Tickets may be obtained on application to the Dean, at 234, Great Portland-street.

McGILL UNIVERSITY, MONTREAL

TRAINING IN PSYCHIATRY

The Department of Psychiatry, McGill University, Montreal, has a limited number of openings for training, and applications are now being considered for 1st July. Applicants must have graduated from an approved medical school and have had a general internship of 1 year.

The 4-year Diploma Course provides general basic preparation during the first 2 years. The last 2 years provide special patterns of instruction for those : (*a*) planning to enter the field of general hospital, community or university psychiatry ; (*b*) preparing themselves for a career in child psychiatry ; (*c*) intending to enter the field of research psychiatry. Credit may be allowed for previous training. Shorter periods of instruction may be arranged, as well as instruction in special fields. Full training in psychoanalysis also may be undertaken within the Department of Psychiatry by suitably prepared candidates. Separate application for this training is required.

All those accepted for training are assigned to 1 of the 7 teaching centres in Montreal. These positions carry with them board and lodging, or, in lieu of lodging, a living-out allowance together with an honorarium ranging from $60 to $150 a month, depending upon the clinical position to which the applicant is assigned. For those in the advanced years of the course, clinical positions carrying higher salaries are available. In several centres, additional emoluments of $1800 a year are available, mainly in the form of bursaries, these being issued under certain conditions in regard to which information will be given on request.

Applicants should write to the Chairman of the Department of Psychiatry, McGill University, Montreal, Canada.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE
(incorporating the Ross Institute)
ROCKEFELLER UNIT OF OCCUPATIONAL HEALTH

A series of 6 WEEKLY LECTURES AND DISCUSSIONS for experienced industrial medical officers will be held at the London School of Hygiene and Tropical Medicine at 6 P.M. on WEDNESDAYS, starting 29TH JANUARY, 1958. Topics to be discussed will include "The Value of Routine Medical Examinations in Industry," "The Medical Implications of Work Study," "The Industrial Medical Officer's Role in the Management of Mental Illness," &c. Admission and refreshments will be free, but limited to ticket-holders.

Further details and applications forms are now available from the Registrar, London School of Hygiene and Tropical Medicine, Keppel-street, W.C.1.

A COURSE OF 10 WEEKLY LECTURES on occupational skin disease will be held for industrial medical officers at the London School of Hygiene and Tropical Medicine by arrangement with the Institute of Dermatology. The lectures will commence at 5.30 P.M. on TUESDAY, 7TH JANUARY, 1958. The course will end with a clinical demonstration at St. John's Hospital on 18TH MARCH. Numbers will be strictly limited. The fee is £3 3s.

Further details and application forms are now available from the Registrar, London School of Hygiene and Tropical Medicine, Keppel-street, W.C.1.

SOCIETY OF APOTHECARIES OF LONDON

DIPLOMA IN INDUSTRIAL HEALTH

The next Examination will begin on MONDAY, 7TH JULY, 1958. The following Examination will be held in DECEMBER, 1958.

For Regulations apply Registrar, Apothecaries' Hall, Black Friars-lane, London, E.C.4.

UNIVERSITY OF TORONTO

FELLOWSHIPS IN MEDICAL RESEARCH AND IN PREVENTIVE MEDICINE

The Col. Sir Albert Gooderham Memorial Fellowship in the Connaught Medical Research Laboratories, University of Toronto.

The Fitzgerald Memorial Fellowship in the School of Hygiene, University of Toronto.

Available to graduates in Medicine or Science—stipends up to $5000 p.a.

For information write to the Director, Connaught Medical Research Laboratories, or the Director, School of Hygiene, University of Toronto.

UNIVERSITY OF CAMBRIDGE. The Appointments Committee of the Faculty of Biology 'B' in the University of Cambridge intend to appoint a UNIVERSITY LECTURER in the Department of Pathology to hold office from 1st October, 1958. Candidates should have had previous experience in the field of virology. The appointment will be subject to the statutes and ordinances of the University.

Details of the post may be obtained from Dr. G. F. ROBERTS, Department of Pathology, Tennis Court-road, Cambridge, to whom candidates should send 10 copies of their applications, together with the names of not more than 3 referees, by 13th February, 1958.

THE UNIVERSITY OF LIVERPOOL. Applications are invited for the post of LECTURER in the Department of Anæsthesia at an initial salary within the range £1200–£1400 p.a., according to qualifications and experience. Clinical facilities will be provided.

Applications, stating age, academic qualifications and experience, together with the names of 3 referees, should be received not later than 1st February, 1958, by the Registrar, from whom further particulars of the conditions of appointment may be obtained.

UNIVERSITY OF OXFORD. Applications are invited for a post of GRADUATE ASSISTANT in the Department of Pathology. The successful candidate will be attached to the morbid anatomy laboratory and will have special responsibility for the museum and the arrangement of demonstrations, &c., in connection with the teaching programme; there will also be opportunities for research. The appointment will be for 1 year in the first instance and preference will be given to candidates with previous experience in pathology. Salary in the range of £900–£50–£1600 according to previous experience and qualifications.

Applications, with the names of 3 referees, should be sent not later than 4th January, 1958, to Dr. A. H. T. ROBB-SMITH, Department of Pathology, Radcliffe Infirmary, Oxford, from whom further particulars may be obtained.

AUSTRALIA. UNIVERSITY OF QUEENSLAND. Applications are invited for appointment to the position of SENIOR LECTURER (CLINICAL) IN MATERIA MEDICA AND THERAPEUTICS in the Department of Medicine. Applicants should hold senior qualifications in clinical medicine, preferably including an M.D. degree, and in addition should have had special experience in therapeutics. Salary £A2160–£A2460 p.a.

Further particulars and application forms may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1. The closing date for the receipt of applications, in Australia and London, is 31st January, 1958.

UNIVERSITY OF OTAGO, Dunedin, New Zealand. A vacancy exists in the Department of Physiology for the position of SENIOR LECTURER or LECTURER.

Salary scales:—
Senior Lecturer: £1790–£2090 p.a. (medically qualified); £1315–£1615 p.a. (science graduate).
Lecturer: £1290–£1590 p.a. (medically qualified); £1025–£1275 p.a. (science graduate).

Further particulars are available from the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1.

Applications close in New Zealand and London on 20th January, 1958.

Hospital Services: Senior Appointments

HOSPITAL OF ST. JOHN AND ST. ELIZABETH, N.W.8. Applications are invited for the post of HONORARY ASSISTANT OBSTETRICIAN AND GYNÆCOLOGIST to the above Hospital. Wide experience and higher qualifications are essential.

Applications (30 copies) should be sent to the undersigned on or before Monday, 10th February, 1958. Testimonials are not required but the names of 3 persons willing to act as referees should be furnished.

Sister MARY CLARE, Secretary,
Hospital of St. John and St. Elizabeth.
60, Grove End-road, London, N.W.8.

AMENDED ADVERTISEMENT

ST. BARTHOLOMEW'S HOSPITAL, E.C.1. Applications are invited for 2 Part-time CONSULTANT appointments in General Surgery. The posts are tenable from 1st October, 1958, and will be for 4 to 6 sessions each per week. Candidates must be in possession of the F.R.C.S. (England).

Applications (12 copies), with the names of 3 referees, should be submitted to the undersigned before 15th January, 1958.

C. C. CARUS-WILSON, Clerk to the Governors.

LEEDS REGIONAL HOSPITAL BOARD.

CONSULTANT in Child Psychiatry (whole-time or maximum part-time). Duties at Child Psychiatric Clinics of the County Boroughs of Wakefield (2 sessions per week), Dewsbury (2 sessions per week) and the remainder with the West Riding County Council (at Mirfield, Wakefield, Goole and Todmorden).

CONSULTANT in Psychiatry (whole-time or maximum part-time). Leeds A and B Groups (mainly at St. James's Hospital). A part-time contract would provide for 5 inpatient and 4 outpatient sessions.

Whole-time ASSISTANT PSYCHIATRISTS (Senior Hospital Medical Officer grade) :—

1. Menston Hospital, near Leeds (2500 Beds) and associated general hospitals. Accommodation for single person only.

2. Storthes Hall Hospital (2680 Beds), Kirkburton, near Huddersfield, and associated general hospitals. Resident or non-resident. Large modern flat available if required. Accommodation also available for a single person.

3. Clifton Hospital, York (1112 Beds), and associated general hospitals. House available.

Candidates for these Senior Hospital Medical Officer posts should normally hold a D.P.M., but applications will also be considered from candidates without previous experience in psychiatry who hold a higher medical qualification, and have had wide experience in general medicine in the Senior Registrar grade and who intend to obtain a D.P.M. and specialise in psychiatry.

Applications (12 copies), stating age, qualifications, and details of present and previous appointments with dates, and names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 21st January, 1958.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

Part-time CONSULTANT SURGEON to Epping Group of hospitals for 5 sessions a week. Residence in Group area desirable. Further particulars on application.

Part-time CONSULTANT PSYCHIATRIST to South Essex Child Guidance Clinic, Whitehall Lodge, Grays, for 2 sessions a week.

Full-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at Runwell Hospital, near Wickford, Essex. Single accommodation available.

Applications (6 copies), and names of 3 referees, should reach the Secretary, 11A, Portland Place, London, W.1, by Saturday, 18th January, 1958.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

Part-time CONSULTANT OPHTHALMOLOGIST to West Ham Group of hospitals for 2 sessions a week. Main duties initially at East Ham Memorial Hospital. Further particulars on application.

Part-time CONSULTANT PHYSICIAN in Endocrinology to the West Ham Group of hospitals for 3 sessions a week (including 1 evening session). Duties to include charge of the Diabetic Clinic at Queen Mary's Hospital, Stratford.

Applications (6 copies), and names of 3 referees, should reach the Secretary, 11A, Portland-place, London, W.1, by Saturday, 25th January.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.

1. CONSULTANT RADIOLOGIST (diagnostic), 3 half-days, Thursday, Friday and Saturday mornings, Willesden General Hospital, Harlesden-road, N.W.10 (127 Beds).

Applications before 3rd February, 1958.

2. ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer grade), 4 half-days a week, Clare Hall Hospital, South Mimms, near Barnet (405 Beds for tuberculous and non-tuberculous chest diseases, including a thoracic surgical unit).

Applications before 5th February, 1958.

Hospitals may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

SHEFFIELD REGIONAL HOSPITAL BOARD. Maximum Part-time CONSULTANT PHYSICIAN required for the Barnsley Group of hospitals.

Application form and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 18th January, 1958.

WELSH REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer), Whitchurch Hospital, near Cardiff. House is available if required.

Applications (12 copies), naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of CONSULTANT PHYSICIAN based at Ballochmyle Hospital, Mauchline, and with duties at other hospitals in the Ayrshire area as may be arranged. The appointment will be whole-time or on the maximum part-time basis of 9 notional half-days per week.

Applications (16 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, not later than 30 days after the publication of this advertisement.

Hospital Services: Junior Appointments

BROOK GENERAL HOSPITAL, Shooters Hill-road, Woolwich, S.E.18. HOUSE PHYSICIAN (pædiatrics and infectious diseases). Vacant mid-January. Not pre-registration. The post is recognised for D.C.H. and entails routine ward and outpatient work including experience in the modern Infectious Diseases Unit and with neonates.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (123 Beds.) Applications are invited for the post of SECOND CASUALTY OFFICER with duties in the Department of Orthopædic and Traumatic Surgery (Senior House Officer grade). Recognised for F.R.C.S. Salary £819 10s. p.a. less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (123 Beds.) Applications are invited for the post of CASUALTY OFFICER AND DEPUTY RESIDENT SURGICAL OFFICER (graded as Senior House Officer). Recognised for F.R.C.S. Salary £819 10s. p.a. less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

DREADNOUGHT SEAMEN'S HOSPITAL, Greenwich, S.E.10 HOUSE PHYSICIAN (pre-registration) required on 21st January.

Applications, stating age, nationality, qualifications and experience, with the names of 3 recent referees, should be sent to the Secretary at the above address not later than 4th January.

GERMAN HOSPITAL, London, E.8. (General—157 Beds.) Applications for the 6-month resident appointment, vacant 29th January, of registered HOUSE PHYSICIAN should reach the Group Secretary, Hackney Hospital, E.9, by 6th January, quoting GH/HS.

GERMAN HOSPITAL, London, E.8. (General—157 Beds.) Applications for the 12-month resident appointment, vacant 27th January, of SENIOR CASUALTY OFFICER (Senior House Officer grade) should reach the Group Secretary, Hackney Hospital, E.9, by 6th January.

FULHAM HOSPITAL, St. Dunstan's-road, Hammersmith, W.6, and FULHAM MATERNITY HOSPITAL, 5/7, Parsons-green, S.W.6. Applications are invited for the joint appointment of REGISTRAR (obstetrics and gynæcology). Post vacant 8th January, 1958. Candidates may visit the Hospitals by arrangement with the Hospital Secretary, Fulham Hospital.

Applications (5 copies) to be submitted by 10th January, 1958, on forms obtainable from, and returnable to, Group Secretary (L.119), 5, Collingham-gardens, London, S.W.5.

HAMPSTEAD GENERAL HOSPITAL, Haverstock Hill, N.W.3. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from suitably qualified medical practitioners for the post of CLINICAL ASSISTANT to the Ophthalmic Department (part-time Medical Officer grade) for 2 sessions a week, Wednesday mornings and Friday mornings.

Application forms may be obtained from the Secretary, to whom they should be returned immediately.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. HOUSE SURGEON required. Vacant 18th January, 1958. Duties mainly orthopædic with some E.N.T. and emergency general surgery. New operating-theatre, outpatient and casualty department. Post recognised for pre-registration service.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

LAMBETH HOSPITAL, Brook-drive, S.E.11. South West METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the post of SURGICAL REGISTRAR for general surgery and genito-urinary work. The appointment is normally for 2 years, but is subject to review at the end of 1 year. The post is resident or non-resident but, if the latter, the successful applicant will be required to sleep in on nights on duty.

Forms of application from the Group Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, to be returned not later than 4th January, 1958.

LONDON HOSPITAL, Whitechapel, E.1, and THE NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of SENIOR REGISTRAR to the Department of Psychiatry. A higher medical qualification, although desirable, is not essential. The successful candidate will spend the first 2 years at The London Hospital and the remainder either at The London Hospital or at a hospital within the Region.

Applications (12 copies), giving the names and addresses of 3 referees, should be received by the undersigned by 8th January, 1958.

H. BRIERLEY, House Governor.

MARIE CURIE HOSPITAL, 66, Fitzjohn's-avenue, Hampstead, N.W.3. HAREFIELD AND NORTHWOOD GROUP HOSPITAL MANAGEMENT COMMITTEE. RESIDENT MEDICAL OFFICER (House Officer grade) required immediately.

Applications, with copies of testimonials, to the Administrative Officer by 31st December, 1957.

MOTHERS' HOSPITAL (SALVATION ARMY), London, E.5. (Maternity—110 Beds.) Applications for the 6-month resident appointment, vacant 1st February, of registered OBSTETRIC HOUSE SURGEON should reach the Group Secretary, Hackney Hospital, E.9, by 6th January, quoting MH/HS.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

MEDICAL REGISTRAR (resident), St. Leonard's Hospital, Nuttall-street, N.1.

REGISTRAR in Orthopædic and Traumatic Surgery (resident or non-resident), King George Hospital, Ilford, Essex. Some duties in Casualty and General Surgical Departments.

ORTHOPÆDIC REGISTRAR (resident or non-resident), Oldchurch Hospital, Romford, Essex. Recognised for F.R.C.S. Post provides excellent experience in diagnosis and treatment of orthopædic and accident cases. Applicants should have had experience in this type of work.

CASUALTY REGISTRAR (resident), Oldchurch Hospital, Romford, Essex.

ANÆSTHETIC REGISTRAR (resident), Chelmsford and Essex and St. John's Hospitals, Chelmsford, Essex, with duties also at Broomfield Hospital, for thoracic surgery. Post recognised for D.A. and F.F.A. R.C.S.

ANÆSTHETIC REGISTRAR (resident or non-resident, an unfurnished bungalow may be available), Black Notley Hospital, Braintree, Essex, and other hospitals in the Colchester Group.

REGISTRAR in Pathology (non-resident for Male, resident or non-resident Female), Southend Group Laboratory, General Hospital, Rochford, Essex. Recognised for Diploma in Pathology.

REGISTRAR in Mental Deficiency (married or single accommodation available), Royal Eastern Counties Hospital, Colchester, Essex. Recognised for D.P.M.

Appointments subject to review after 1 year.

Application forms from Secretary, 11A, Portland-place, W.1, to be returned by 11th January, 1958.

NORTH MIDDLESEX HOSPITAL, London, N.18. Applications are invited from pre- and post-registration candidates for the post of RESIDENT HOUSE SURGEON (general, orthopædic, and traumatic surgery). 6-month appointment from mid-January. Recognised for F.R.C.S.

Applications, giving full particulars, together with copies of recent testimonials, to Hospital Secretary, by 1st January.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. ANÆSTHETIST (Senior House Officer). Resident post tenable for 6 months in the first instance from a date as soon after 1st January, 1958, as can be arranged, for duties at both Hospitals. Post recognised for the purpose of the F.F.A. R.C.S.

Applications to the House Governor immediately on forms obtainable from 339, Goldhawk-road, London, W.6.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. ANÆSTHETIST (Senior House Officer), resident post tenable for 6 months from 1st April, 1958, in the first instance, for duties at both hospitals. Post recognised for the purpose of the F.F.A. R.C.S.

Applications to the House Governor by 13th January, 1958, on forms obtainable from 339, Goldhawk-road, London, W.6.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. QUEEN CHARLOTTE'S MATERNITY HOSPITAL. JUNIOR OBSTETRIC OFFICER (Senior House Officer), resident post, tenable for 6 months from 1st April, 1958.

Applications to the House Governor by 13th January, 1958, on forms obtainable from 339, Goldhawk-road, London, W.6.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. CHELSEA HOSPITAL FOR WOMEN. HOUSE SURGEON (Senior House Officer), resident post, tenable for 1 year from 1st April, 1958.

Applications to the House Governor by 13th January, 1958, on forms obtainable from 339, Goldhawk-road, London, W.6.

ROYAL NORTHERN HOSPITAL, Holloway, N.7. Applications are invited for the post of CASUALTY OFFICER (Senior House Officer grade), with duties in the Ophthalmic Department, vacant 26th January, 1958. Recognised for F.R.C.S.

Applications to be sent to the Hospital Secretary by 7th January, 1958.

SPRINGFIELD HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required. The Hospital is a large one and offers excellent experience in diagnosis and treatment of all forms of mental disorder including the neuroses. Every variety of modern treatment is carried out in a well equipped treatment centre. Single accommodation is available. Candidates may visit the Hospital by arrangement.

Apply to Group Secretary, Springfield Hospital, Tooting, S.W.17, for application forms which should be returned duly completed on or before 18th January, 1958.

ST. MARY ABBOTS HOSPITAL, Marloes-road, Kensington, W.8. Applications are invited for appointment to the Urology Department of a REGISTRAR (part-time), 5 sessions a week.

Applications (5 copies) to be submitted by 10th January, 1958, on forms obtainable from, and returnable to, Group Secretary, 5, Collingham-gardens, London, S.W.5. (L.118.)

ST. STEPHEN'S HOSPITAL, Chelsea, S.W.10. Paediatric HOUSE PHYSICIAN (with some dermatology duties). Resident. Vacancy 22nd January, 1958.

Applications, naming 2 referees, to Medical Superintendent within 14 days.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, London, W.C.1. SENIOR MEDICAL REGISTRAR (non-resident) required at the Hospital for Tropical Diseases, 4, St. Pancras-way, N.W.1, for 1 year in the first instance from 1st March, 1958.

Applications, with names of 2 referees, to T. F. W. MACKEOWN, Administrator and Secretary, University College Hospital, by 8th January, 1958.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, W.C.1. Applications are invited for the appointment of SURGICAL REGISTRAR for 1 year in the first instance from a date to be arranged. The successful candidate will be required to undertake a period of duty at the National Temperance Hospital, Hampstead-road, N.W.1.

Applications, with names of 2 referees, to T. F. W. MACKEOWN, Administrator and Secretary, University College Hospital, by the 10th January, 1958.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. (Acute general—192 Beds.) Applications are invited from registered or provisionally registered medical practitioners for the post of HOUSE SURGEON.

Applications, with copies of 2 testimonials, to the Hospital Secretary by 3rd January, 1958.

WANSTEAD HOSPITAL, Hermon Hill, E.11. (191 Beds.) Applications are invited for the post of CASUALTY OFFICER (recognised for F.R.C.S.), graded Senior House Officer. Vacant 1st January, 1958. Salary £819 10s. p.a. less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WANSTEAD HOSPITAL, Hermon Hill, London, E.11. (191 Beds.) HOUSE SURGEON required. Recognised for F.R.C.S.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WESTERN HOSPITAL, Seagrave-road, Fulham, S.W.6. Applications are invited for appointment as REGISTRAR (infectious diseases). Post vacant 26th March, 1958. The Hospital is the regional centre for the treatment of respiratory complications of poliomyelitis, and has facilities for research. Candidates may visit the Hospital by arrangement with the Physician-Superintendent.

Applications (5 copies) to be submitted by 10th January, 1958, on forms obtainable from, and returnable to, Group Secretary (L.120), 5, Collingham-gardens, London, S.W.5.

BARNSLEY. BECKETT HOSPITAL. Applications are invited for the post of RESIDENT HOUSE SURGEON (surgical), pre-registration post. Vacant now. The post offers excellent facilities for gaining experience.

Applications, naming 2 referees, to the Group Secretary, Barnsley Hospital Management Committee, 33, Gawber-road, Barnsley.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE SURGEON (pre-registration); vacant now. The Hospital serves a wide area of pleasant countryside and the post affords good opportunity to study excellent clinical material.

Apply to Group Secretary, 19, Alexandra-road, Barnstaple.

BEDFORD GENERAL HOSPITAL. (436 Beds.) Applications are invited for the following posts :—

HOUSE SURGEON post, vacant immediately. Pre- or post-registration ; recognised for F.R.C.S. Post offers exceptional opportunities for general experience in busy acute surgical units.

ORTHOPÆDIC HOUSE SURGEON post, vacant immediately. Pre- or post-registration ; recognised for F.R.C.S. Post offers wide experience in a busy specialist orthopædic and traumatic unit.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 Beds.) HOUSE PHYSICIAN (House Officer or Senior House Officer grading according to experience).

Apply Group Secretary.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 acute beds.) SENIOR HOUSE OFFICER in Obstetrics and Gynæcology. Vacant soon. Hospital has Maternity Unit of 22 beds and Gynæcological Annexe of 18 beds. Married quarters may be available.

Detailed applications to Group Secretary.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) SENIOR HOUSE OFFICER (anæsthetics). Post recognised for F.F.A. R.C.S. and D.A. and vacant from mid-December. This is a busy general hospital offering a sound and varied experience in anæsthetics.

Applications, giving age, qualifications, experience and the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BIRMINGHAM ACCIDENT HOSPITAL, Bath-row, BIRMINGHAM, 15. (215 Beds and 8 House Surgeons.) HOUSE SURGEONS (resident). Vacant January/February. Hospital is largest traumatic unit in country and treats over 50,000 new patients each year. Recognised for purpose of casualty by R.C.S. (Eng.). Teaching programme by consultant staff. 6-month appointment, some of which may be spent in 42-Bedded Medical Research Council's Burns Unit.

Apply, naming 2 referees, to Administrator.

BIRMINGHAM, 9. LITTLE BROMWICH GENERAL HOSPITAL. HOUSE PHYSICIAN (Male/Female). Vacant 12th January, 1958. Pre-registration post.

Apply Physician-Superintendent with copies of 2 testimonials or names of referees.

BIRMINGHAM, 9. LITTLE BROMWICH GENERAL HOSPITAL. HOUSE SURGEON (Male/Female). Vacant 7th January, 1958. Pre-registration post.

Apply Physician-Superintendent with copies of 2 testimonials or names of referees.

BIRMINGHAM. SOLIHULL HOSPITAL, Lode-lane, SOLIHULL. HOUSE PHYSICIAN (pre-registration). Vacant January. General hospital offering good experience. 5 other resident medical staff.

Applications, with names of 2 referees, to Medical Superintendent as soon as possible.

BIRMINGHAM. SOLIHULL HOSPITAL, Lode-lane, SOLIHULL. RESIDENT MEDICAL OFFICER (Senior House Officer). Vacant end of January. General hospital with 5 other resident medical officers.

Apply Medical Superintendent.

BIRMINGHAM. SOLIHULL HOSPITAL, Lode-lane, SOLIHULL. HOUSE SURGEON (pre-registration). Vacant January. General hospital offering good experience. 5 other resident medical staff.

Applications, with names of 2 referees, to Medical Superintendent immediately.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS AND THE BIRMINGHAM REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time post of NON-RESIDENT DERMATOLOGICAL REGISTRAR (Senior Registrar or Registrar grade). Duties will include sessions at the Queen Elizabeth Hospital and other units of the United Birmingham Hospitals, and at hospitals of the Birmingham Regional Hospital Board. Candidates must be registered medical practitioners and have had previous experience in the specialty. For appointment to Senior Registrar grade, candidates should possess the M.R.C.P.

Forms of application may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned not later than 11th January, 1958.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the post of REGISTRAR in Radiodiagnosis (non-resident), Registrar grade, for duty in the United Hospitals. The successful candidate will be given an opportunity to attend a course of instruction for the Diploma in Medical Radiology (diagnostic—part I) at an approved centre for which purpose a bursary is provided.

Application forms may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, and should be returned to him by 4th January, 1958.

BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

The Royal Infirmary, Bolton (238 Beds)

RESIDENT SENIOR HOUSE OFFICER in Orthopædic Surgery. Vacant 1st February, tenable for 12 months and recognised for F.R.C.S.

RESIDENT HOUSE SURGEONS (3). Vacant 15th January, 16th January and 1st February, tenable for 6 months and recognised under pre-registration service scheme. Also recognised for F.R.C.S.

Bolton District General Hospital (607 Beds)

RESIDENT SENIOR HOUSE OFFICERS in Medicine (2). 1 vacant immediately and 1 in New Year. Both tenable for 12 months.

RESIDENT HOUSE PHYSICIANS (3). 1 vacant immediately, 1 23rd January, and 1 14th February. Tenable for 6 months and recognised under pre-registration service scheme.

RESIDENT HOUSE SURGEONS (2). 1 vacant immediately and 1 8th February, tenable for 6 months and recognised under pre-registration service scheme. Also recognised for F.R.C.S.

Applications, stating age, nationality, qualifications, experience and the names of 2 referees, to Group Secretary, The Royal Infirmary, Bolton.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the appointment of HOUSE SURGEON (recognised for F.R.C.S.) to the General Surgical Unit (60 Beds). The post will be vacant on the 1st February, 1958. Salary in accordance with national scale. The post is recognised as a pre-registration appointment.

Applications, stating age, qualifications, experience, and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton, 7.

BRIGHTON. ROYAL ALEXANDRA HOSPITAL FOR SICK CHILDREN, Dyke-road. (130 Beds.) BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE. Vacancies for HOUSE PHYSICIAN and HOUSE SURGEON for 6 months from 17th January and 14th February, 1958, respectively. Both posts offer wide experience in pædiatrics and are recognised for D.C.H. That of House Surgeon is open to pre-registration candidates.

Applications, stating age, nationality, qualifications and experience, together with copies of recent testimonials, to be sent to the Administrative Officer as soon as possible.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. SENIOR CASUALTY OFFICER (Junior Hospital Medical Officer), non-resident, required mid-December, at the above Hospital. Recognised for F.R.C.S.

Applications as locum or for permanent post, stating usual particulars and the names of 2 referees, to the Administrative Officer.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) HOUSE SURGEON (including gynæcology) required 1st February, 1958. Pre-registration and recognised for F.R.C.S.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BROMSGROVE, WORCESTERSHIRE. HILL TOP HOSPITAL (76 Beds.) REGIONAL THORACIC SURGICAL CENTRE. Applications are invited for the pre-registration post of HOUSE PHYSICIAN at the above Hospital. Post vacant January, 1958.

Applications, with the names of 3 referees, to the Hospital Secretary, Bromsgrove General Hospital, Worcestershire.

BROMSGROVE, WORCESTERSHIRE. HILL TOP HOSPITAL. (76 Beds.) REGIONAL THORACIC SURGICAL CENTRE. Applications are invited for the pre-registration post of HOUSE SURGEON at the above Hospital. Post vacant January, 1958.

Applications, with the names of 3 referees, to the Hospital Secretary, Bromsgrove General Hospital, Bromsgrove, Worcestershire.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road, BOSCOMBE. (494 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (orthopædics and casualty combined), resident or non-resident, required for the end of December. The post is recognised for the F.R.C.S. examination and is normally tenable for 12 months. The Unit consists of a Registrar and 2 Senior House Officers with an additional Senior House Officer during the summer months.

Applications to the Hospital Secretary.

BRADFORD A AND B HOSPITAL MANAGEMENT COMMITTEES. JUNIOR HOUSE OFFICER required for Geriatric Admission Unit. Post vacant 1st February, 1958. Major portion of duties carried out at St. Luke's Hospital, Bradford.

Applications, stating age, nationality, qualifications and experience, and copies of testimonials, to the Secretary, Royal Infirmary, Bradford, Yorks.

BURTON-ON-TRENT. THE GENERAL HOSPITAL. HOUSE SURGEON (general—pre-registration) required at the above Hospital immediately. Post recognised for F.R.C.S.

Applications to Group Secretary as soon as possible.

BURTON-ON-TRENT. THE GENERAL HOSPITAL. HOUSE SURGEON (orthopædics), for work in Casualty Department, required immediately. Flat available for married officer without children.

Applications to Group Secretary as soon as possible.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. BURY GENERAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER in Casualty and Orthopædics. This post is recognised for the F.R.C.S.

Full details, including nationality, age, qualifications and experience, with the names of 2 referees, should be forwarded to H. WILKINSON, Group Secretary, Bury General Hospital, Bury, Lancs.

BURY ST. EDMUNDS. WEST SUFFOLK GENERAL HOSPITAL. (262 Beds.) Applications are invited for the following posts:

(*a*) HOUSE OFFICER (pre-registration) or SENIOR HOUSE OFFICER for Orthopædic and Casualty duties; recognised for F.R.C.S. (surgical). Vacant January. A Junior Hospital Medical Officer is also employed.

(*b*) Locum tenens HOUSE SURGEONS (pre-registration) required for (i) Gynæcological and Obstetric duties and (ii) Orthopædic and Casualty duties for periods during the first 3 weeks of January.

Applications, with testimonials or names of 3 referees, to Hospital Secretary (Telephone: Bury St. Edmunds 2381).

BUXTON. DEVONSHIRE ROYAL HOSPITAL. (252 Beds.) Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER, vacant now. This Hospital is a large special hospital for the treatment and rehabilitation of all types of locomotor disorders. Duties are mainly medical and include work in the long-stay unit of the Manchester University Rheumatism Research Centre. The Hospital is recognised under the regulations for the Diploma in Physical Medicine, Part II, and the post also offers good medical experience.

Applications, stating age, experience and qualifications, together with the names of 2 persons for reference, to be addressed to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport, immediately.

CAMBRIDGE. THE UNITED CAMBRIDGE HOSPITALS. ADDENBROOKE'S HOSPITAL, CAMBRIDGE. HOUSE SURGEON (in Orthopædic Department) for 6 months from 8th February. Recognised pre-registration service.

Apply to the Secretary immediately, stating age, nationality, qualifications and experience with dates, and with copies of 3 testimonials. Interviews mid-January.

CAMBRIDGE. THE UNITED CAMBRIDGE HOSPITALS. ADDENBROOKE'S HOSPITAL, CAMBRIDGE. HOUSE SURGEONS (2) for 6 months from mid-February. Recognised pre-registration service.

Apply to the Secretary by 4th January, stating age, nationality, qualifications and experience with dates, and with copies of 3 testimonials. Interviews late January.

CAMBRIDGE. THE UNITED CAMBRIDGE HOSPITALS. ADDENBROOKE'S HOSPITAL, CAMBRIDGE. HOUSE OFFICER (E.N.T. Department) for 6 months from mid-February. Pre-registration (surgical) or post-registration applications will be considered.

Apply to the Secretary by 4th January, stating age, nationality, qualifications, and experience with dates, and with copies of 3 testimonials. Interviews late January.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of SENIOR HOUSE PHYSICIAN will be vacant at Stodmarsh-road Annexe early in January, 1958; duties will include care of 30-Bedded unit of chest diseases, also work at the chest clinic and with the pneumoconiosis unit. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CARLISLE. CUMBERLAND INFIRMARY, CITY GENERAL HOSPITAL AND CITY MATERNITY HOSPITAL. Applications are invited for the following appointments which are vacant as from 1st February, 1958:—

HOUSE OFFICERS, recognised for pre-registration purposes. Period 6 months.

3 general surgery (recognised for F.R.C.S. examination).
1 general medicine.
2 obstetrics and gynæcology (1 recognised for D.Obst.R.C.O.G. examination).

SENIOR HOUSE OFFICERS. Period 12 months.

1 general surgery (recognised for F.R.C.S. examination).
1 general medicine.
1 orthopædics.
1 E.N.T.

Apply to the Group Secretary, Cumberland Infirmary, Carlisle.

CARDIFF. THE UNITED CARDIFF HOSPITALS. Applications are invited for the appointment of SENIOR REGISTRAR in General Medicine at the Cardiff Royal Infirmary. Non-resident appointment, to commence 1st February or as soon afterwards as possible.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

CARDIFF. THE UNITED CARDIFF HOSPITALS. Applications are invited for the appointment of SENIOR HOUSE OFFICER in General Medicine at the Cardiff Royal Infirmary, to commence 1st February, 1958. The post combines the duties of Resident Medical Officer at the Infirmary, and resident accommodation (a single flat) is available.

Application forms are obtainable from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

CARMARTHEN. WEST WALES GENERAL HOSPITAL. (188 Beds.) WEST WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of pre-registration HOUSE OFFICER (medical) which will become vacant on 1st February, 1958. Salary and conditions of service as laid down by the Ministry of Health.

Applications, stating age, qualifications, experience and nationality, with names and addresses of 3 referees, to the Group Secretary, West Wales Hospital Management Committee, Glangwili, Carmarthen.

CARMARTHEN. WEST WALES GENERAL HOSPITAL. (188 Beds.) WEST WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of pre-registration HOUSE OFFICER (surgical) (recognised by the Royal College of Surgeons, and for pre-registration service), which will become vacant on 1st February, 1958. Salary and conditions of service as laid down by the Ministry of Health.

Applications, stating age, qualifications, experience and nationality, with names and addresses of 3 referees, to the Group Secretary, West Wales Hospital Management Committee, Glangwili, Carmarthen.

CARMARTHEN. WEST WALES GENERAL HOSPITAL. (188 Beds.) WEST WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (orthopædic and traumatic surgery) (recognised by the Royal College of Surgeons) which is now vacant. Salary and conditions of service as laid down by the Ministry of Health.

Applications, stating age, qualifications, experience, nationality, and names and addresses of 3 referees, to the Group Secretary, West Wales Hospital Management Committee, Glangwili, Carmarthen.

CASTLEFORD, NORMANTON AND DISTRICT HOSPITAL, Hightown, Castleford. RESIDENT SURGICAL OFFICER (Senior House Officer grade) required. Married accommodation available. Post vacant 1st January, 1958.

Applications as soon as possible to the Secretary, Pontefract and Castleford Hospital Management Committee, Great Northern House, Salter-row, Pontefract, Yorkshire.

CHELMSFORD AND ESSEX HOSPITAL. (161 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON. Pre-registration post. The post offers good surgical experience. Recognised for the F.R.C.S.

Applications, together with 2 recent testimonials, to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHELMSFORD AND ESSEX AND ST. JOHN'S HOSPITALS. Resident Locum ANÆSTHETIC REGISTRAR required.

Applications to Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford, Essex.

CHICHESTER. ROYAL WEST SUSSEX HOSPITAL. (202 acute beds.) SENIOR HOUSE SURGEON (Deputy Resident Surgical Officer) required at above Hospital. Post recognised for F.R.C.S. Resident staff of 6—Resident Surgical Officer, 3 House Surgeons, Resident Medical Officer, and House Physician. Salary £819 10s. p.a., less residential charge. Vacant 28th December, 1957.

Applications, stating age, experience, qualifications, with references or names of referees, to Senior Administrative Officer.

CHICHESTER. ST. RICHARD'S HOSPITAL. (400 Beds.) CHICHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, HOUSE SURGEON (pre-registration), for 6 months only in the first instance. Post vacant 1st January, 1958. The man or woman appointed will work primarily in the surgical wards of the Hospital. Hospital recognised for F.R.C.S.

Applications, stating age, qualifications and experience, giving names of 2 persons from whom reference may be obtained, should be sent to the Surgeon-Superintendent.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for :—

Essex County Hospital, Colchester (189 Beds)

Post of HOUSE PHYSICIAN. First, second, third or pre-registration post, tenable for 6 months.

Essex County Hospital, Colchester (19 gynæcological beds), **Colchester Maternity Hospital** (22 obstetric beds)

Post of HOUSE OFFICER (Male or Female) (obstetric and gynæcological). First, second, third or pre-registration post, tenable for 6 months.

Black Notley Hospital, Braintree, Essex (516 Beds)

Post of HOUSE SURGEON. Includes duties in general surgical and gynæcological wards. Recognised for F.R.C.S.

Post of HOUSE PHYSICIAN. Includes duties in medical and pædiatric wards. First, second, third or pre-registration posts; tenable for 6 months.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Group Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botleys Park War Hospital). (430 Beds.) SENIOR HOUSE OFFICER ANÆSTHETIST required February, 1958. Appointment recognised for D.A. and F.F.A. R.C.S. Salary in accordance with terms and conditions of National Health Service.

Applications, together with names and addresses of referees, to Physician-Superintendent, St. Peter's Hospital, as soon as possible.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botleys Park War Hospital). (430 Beds.) RESIDENT HOUSE SURGEON (Senior House Officer or Intern) required for Gynæcological (30 Beds) and E.N.T. (approximately 14 Beds) Departments. Salary in accordance with terms and conditions of National Health Service. Post vacant 1st February, 1958.

Applications, together with names and addresses of referees, to Physician-Superintendent, St. Peter's Hospital, as soon as possible.

CHESTER. BARROWMORE HOSPITAL, Great Barrow, CHESTER. Male SENIOR HOUSE OFFICER (medical) required. Salary £819 10s. p.a., less £150 for residence. The Hospital is modern and for the treatment of pulmonary tuberculosis. It contains a regional thoracic surgical unit and a general chest ward. Applications from ex-patients considered.

Inquiries and applications, stating names of 2 referees, to be sent to Physician-Superintendent.

CREWE AND DISTRICT MEMORIAL HOSPITAL. (140 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (surgical), vacant 26th January, 1958, which is recognised by the Royal College of Surgeons for the F.R.C.S. examination. This hospital has recently had a new twin theatre suite, and a new large Casualty Department added. There are 7 residents and ample opportunity for gaining experience in operative surgery will be afforded to the right candidate. Salary and conditions in accordance with Whitley Council scale.

Applications, stating age, qualifications, &c., with names of 2 referees, to be sent to the Group Secretary, Barony Hospital, Nantwich, Cheshire, within 10 days after publication.

CROWTHORNE, BERKSHIRE. BROADMOOR INSTITUTION. (920 Beds for persons of unsound mind of criminal tendencies.) SENIOR REGISTRAR. House or quarters available.

Applications, naming 3 referees, to Medical Superintendent by 18th January, 1958. Candidates may visit Hospital by appointment.

DEWSBURY, YORKSHIRE. THE GENERAL HOSPITAL. Applications are invited for the pre-registration post of HOUSE PHYSICIAN (general medicine and pædiatrics) which falls vacant on 1st February, 1958.

Applications, with full details, to the Administrative Officer at the Hospital.

DEWSBURY, YORKSHIRE. THE GENERAL HOSPITAL. Applications are invited for the immediate vacancy of HOUSE OFFICER (general surgery).

Applications, giving full details, to the Administrative Officer at the Hospital.

DORCHESTER. DORSET COUNTY HOSPITAL. (109 Beds.) HOUSE SURGEON required for resident, pre-registration post vacant mid-January and tenable for 6 months. Recognised for F.R.C.S. examinations.

Applications, stating age and qualifications, together with copy testimonials, to Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset, immediately.

DURHAM. COUNTY HOSPITAL. (116 Beds.) Senior HOUSE OFFICER in Orthopædics required immediately. Resident. The County Hospital is the main Orthopædic and Accident Hospital in a busy mining and industrial area. Experience can be obtained in all branches of orthopædics.

Applications, with particulars of previous experience and names of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.

1. REGISTRAR (plastic surgery), Regional Plastic Surgery and Burns Unit, West Norwich Hospital (Norfolk and Norwich Hospital Group). Post offers wide experience and training. Appointment for 1 year, renewable for second year. Candidates invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary, Norfolk and Norwich Hospital, Norwich.

2. REGISTRAR (medical), Newmarket General Hospital. Post provides good experience in general medicine and diseases of the chest. Previous experience of tuberculosis an advantage. House available. Appointment for 1 year, renewable for second year. Candidates invited to visit Hospital by direct arrangement with the Physician-Superintendent.

3. REGISTRAR (radiological), Ipswich and East Suffolk Hospital (Anglesea-road Wing), Ipswich. The department is the centre for consultant radiological services for the Ipswich Hospital Group. Post recognised for D.M.R.D. Part II examination. Appointment for 1 year, renewable for second year. Candidates invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary at the Hospital.

Applications, stating age, experience, and the names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, to be returned by 13th January, 1958.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT HOUSE SURGEON required 12th February. Pre-registration post, recognised for F.R.C.S.

Applications, stating age, qualifications, and experience, with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. Applications are invited from registered medical practitioners for the appointment of RESIDENT MEDICAL OFFICER (with duties as Senior House Officer to the Neurologist). Vacant 1st February, 1958.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary by 11th January, 1958.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. Applications are invited from registered medical practitioners (Male and Female) for the appointment of SENIOR HOUSE OFFICER in Clinical Pathology (resident). Vacant now. The successful candidate will be responsible for emergency pathological and blood-transfusion duties, and will receive training in the different branches of clinical pathology.

Applications, with names of 2 referees, to the Hospital Secretary immediately.

EXETER. ROYAL DEVON AND EXETER HOSPITAL invites applications from pre-registration and registered medical practitioners for the appointment of HOUSE PHYSICIAN. Vacant 9th February, 1958.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary by 4th January, 1958.

GRAVESEND AND NORTH KENT HOSPITAL, Gravesend, Kent. Locum ORTHOPÆDIC REGISTRAR required for a period of approximately 16 weeks from 9th January, 1958.

Applications immediately to Group Secretary, Medway and Gravesend Hospital Management Committee, 20, Star Hill, Rochester.

GRAVESEND AND NORTH KENT HOSPITAL, Gravesend. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON. Applications are invited for this resident post, vacant early January; approved under pre-registration regulations and tenable for 6 months. Post offers experience also in obstetrics, gynæcology, and orthopædics. Salary £467 10s.–£577 10s. p.a., according to experience.

Applications to Hospital Secretary, giving details of experience, age, qualifications, and nationality.

GREENOCK. GATESIDE INFECTIOUS DISEASES HOSPITAL. BOARD OF MANAGEMENT FOR GREENOCK AND DISTRICT HOSPITALS. Applications are invited from suitably qualified medical practitioners for the appointments of RESIDENT JUNIOR HOSPITAL MEDICAL OFFICERS. Good experience offered in the diagnosis and treatment of infectious diseases including venereal diseases. Well equipped clinical laboratory. The appointments will be subject to the National Health Service (Scotland) (superannuation) regulations.

Applications, giving details of age, experience, and qualifications, together with copies of 3 recent testimonials, or names of referees, should be forwarded to the Group Secretary and Treasurer, 47 Eldon-street, Greenock, within 14 days from date of insertion.

GUILDFORD. ROYAL SURREY COUNTY HOSPITAL. RESIDENT HOUSE SURGEON required for General Surgery. Post is vacant on 13th January and tenable for 6 months. It is approved for pre-registration candidates and recognised for the F.R.C.S. examination.

Applications, with copies of 3 testimonials, should be sent to the Hospital Secretary as soon as possible.

HASTINGS AND ST. LEONARDS-ON-SEA. BUCHANAN HOSPITAL. (91 Beds.) (Obstetric, Gynæcological and Premature Baby Unit.) SENIOR HOUSE OFFICER required for Obstetric and Premature Baby Unit. Appointment, recognised for D.Obst.R.C.O.G., is vacant 17th January, 1958.

Apply, giving names and addresses of 3 referees, to Hospital Administrator.

HASTINGS GROUP HOSPITAL MANAGEMENT COMMITTEE. Locum SENIOR HOUSE OFFICER (anæsthetics) required for duties within the Group. Married quarters available if required. Post vacant from 1st January, 1958. Salary £15 19s. per week.

Apply to Group Secretary, 11, Holmesdale-gardens, Hastings, giving details of qualifications, experience, and names of referees.

HASTINGS. ST. HELEN'S HOSPITAL. (493 Beds.) HOUSE SURGEON required. Pre-registration post recognised for F.R.C.S. Modern theatre. Staff of 4. Vacant 16th January, 1958.

Applications to Hospital Administrator by 1st January.

HAVERFORDWEST. PEMBROKE COUNTY WAR MEMORIAL HOSPITAL. (163 Beds.) WEST WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (general surgery) (recognised by the Royal College of Surgeons). Salary and conditions of service as laid down by the Ministry of Health.

Applications, stating age, qualifications, experience and nationality, with names and addresses of 3 referees, to the Group Secretary, West Wales Hospital Management Committee, Glangwili, Carmarthen.

HAVERFORDWEST. PEMBROKE COUNTY WAR MEMORIAL HOSPITAL. (163 Beds.) WEST WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of pre-registration HOUSE OFFICER (surgical) (recognised by the Royal College of Surgeons, and for pre-registration service), which will become vacant on 1st February, 1958. Salary and conditions of service as laid down by the Ministry of Health.

Applications, stating age, qualifications, experience and nationality, with names and addresses of 3 referees, to the Group Secretary, West Wales Hospital Management Committee, Glangwili, Carmarthen.

HEMEL HEMPSTEAD, HERTFORDSHIRE. WEST HERTS HOSPITAL. HOUSE SURGEON (pre-registration) required.

Applications, giving full details and 2 names for reference, should be sent to the Hospital Secretary as soon as possible.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) Applications are invited for the post of CASUALTY OFFICER. The post, which is resident, is recognised under the Fellowship regulations and will be graded either Junior Hospital Medical Officer or Senior House Officer according to experience. Duties terminate at 7 P.M. with 1 night weekly on call.

Applications for the appointment, which will be vacant on 23rd January, 1958, should be accompanied by copies of 3 recent testimonials and addressed to the undersigned.

H. J. JOHNSON, Group Secretary.

The Royal Infirmary, Huddersfield.

HEREFORD. COUNTY HOSPITAL. (335 Beds.) HOUSE OFFICER (surgery) required. Hospital recognised for F.R.C.S. Post vacant 15th January, 1958.

Applications, with copies of 2 recent testimonials, to Medical Superintendent, County Hospital.

HERTFORD COUNTY HOSPITAL. (171 Beds. Hospital situated 21 miles from London.) Applications are invited for the appointment of HOUSE SURGEON (general, gynæcology and obstetrics). First or second post. To commence as soon as possible. Pre-registration post; recognised under F.R.C.S. regulations.

Applications to Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

HOUNSLOW HOSPITAL, Staines-road, Hounslow, MIDDLESEX. (General, acute—81 Beds.) Applications are invited for the appointment of RESIDENT HOUSE PHYSICIAN. Recognised pre-registration appointment for 6 months. Vacant 14th December, 1957.

Applications, stating qualifications and age, together with copies of up to 3 recent testimonials or names for reference, to the Hospital Secretary.

HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in the E.N.T. Department of the Victoria Hospital for Sick Children and the Hull Royal Infirmary. The post, which is now vacant, is recognised for the F.R.C.S. and D.L.O.

Applications, with testimonials, should be sent to the Hospital Secretary, Victoria Hospital for Sick Children, Park-street, Hull.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE PHYSICIAN. Duties in an active geriatric unit for the investigation and treatment of acute and long-term illness. Resident post.

Applications, with full particulars, to the Hospital Secretary.

HULL. VICTORIA HOSPITAL FOR SICK CHILDREN, Park-street. SENIOR HOUSE OFFICER required to commence on 3rd February, 1958. Duties are those of Casualty Officer and offer good experience. The successful candidate will be expected to supervise the other Junior House Officers.

Apply, giving testimonials, to the Hospital Secretary at the above address.

ILFORD. KING GEORGE HOSPITAL. There will be a vacancy for a CASUALTY OFFICER at above Hospital on 27th January, 1958, at a salary of £819 10s. p.a., resident or non-resident. Senior House Officer grade. This post is recognised for the F.R.C.S.

Applications, giving full particulars and accompanied by testimonials, should be sent to the undersigned within seven days of the appearance of this advertisement.

H. F. HARRIS, Group Secretary, Ilford and Barking Group Hospital Management Committee.

King George Hospital, Ilford.

ILKLEY. MIDDLETON HOSPITAL. (430 Beds.) Resident JUNIOR HOSPITAL MEDICAL OFFICER required at the above Hospital. This appointment provides for experience in the specialties of tuberculosis and geriatrics.

Applications, stating age, nationality, qualifications and experience, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (356 Beds.) Applications are invited for the post of HOUSE SURGEON to the Senior Consultant General Surgeon, vacant mid-January. The post is recognised for pre-registration and for the F.R.C.S. examinations.

Applications, with copies of recent testimonials, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (356 Beds.) Applications are invited for 2 posts of HOUSE SURGEON to Consultant General Surgeons, both vacant mid-January. The posts are recognised for pre-registration and for the F.R.C.S. examinations.

Applications, with copies of recent testimonials, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Heath-road WING), IPSWICH. (280 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER to the Fracture and Orthopædic Department. The post, which becomes vacant at the end of January, is recognised for the R.C.S. examinations.

Applications, with full details and copies of recent testimonials, to the Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Heath-road WING), IPSWICH. Applications invited for 2 posts of HOUSE SURGEON, pre-registration, to general surgeons. Posts become vacant on 7th and 17th January, 1958, and are recognised for F.R.C.S. examination.

Detailed applications, with copies of recent testimonials, to Hospital Secretary.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. House PHYSICIANS (2), pre-registration, required for General Medical Units. Vacant 5th and 10th February.

Applications, stating age, nationality, qualifications, with copies of up to 2 testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 8th January.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. House SURGEON, General Surgical Unit. Vacant 17th February.

Applications, stating age, qualifications and nationality, with copies of up to 2 recent testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 7th January.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. House SURGEON (pre-registration), General Surgery Unit. Vacant 1st February.

Applications, stating age, qualifications and nationality, with copies of up to 2 recent testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 7th January.

KETTERING AND DISTRICT GENERAL HOSPITAL. CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. The post, vacant December, 1957, offers wide experience of all traumatic conditions including fractures and some orthopaedic cases with charge of 30 beds.

Applications, accompanied by testimonials, to be sent to the Group Secretary, General Hospital, Kettering.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-on-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of Locum SENIOR HOUSE OFFICER (orthopædic and casualty) for approximately 1 month from 20th January, 1958.

Applications, stating age, qualifications, and experience, with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital as soon as possible.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-UPON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the posts of HOUSE OFFICER (general surgery), 2 posts (pre-registration), which are available on 1st February, 1958.

Applications, stating age, qualifications and experience, with 2 recent testimonials, should reach the Physician-Superintendent of the hospital within 7 days of the appearance of this advertisement.

LANARK. BELLEFIELD SANATORIUM. Resident JUNIOR HOSPITAL MEDICAL OFFICER required for above Sanatorium.

Applications to the Secretary, Board of Management for Glasgow Victoria Hospitals, 24, St. Vincent-place, Glasgow, C.1.

LEEDS. THE UNITED LEEDS HOSPITALS. Applications are invited for the post of RESIDENT MEDICAL OFFICER at the General Infirmary at Leeds. The post is of Registrar status and will be tenable for 1 year from 1st January, 1958, in the first instance.

Applications, stating age, qualifications, previous posts with dates, and 3 names for reference, should be forwarded to the Sub-Dean, School of Medicine, Leeds, 2, by not later than 31st December, 1957.

LEICESTER ROYAL INFIRMARY (492 Beds) and GENERAL HOSPITAL (454 Beds). SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (orthopædics) required. Appointment for 1 year in first instance, Leicester General Hospital (72 orthopædic beds), Leicester Royal Infirmary (54 orthopædic beds).

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 6th January, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LLANELLY HOSPITAL, Llanelly. Glantawe Hospital MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the resident appointment of JUNIOR HOSPITAL MEDICAL OFFICER in the Medical Unit of the above Hospital.

Applications stating age, experience and qualifications, together with copies of 2 recent testimonials, should be sent to the Secretary of the Hospital. T. E. JONES, Group Secretary.

LYMINGTON HOSPITAL, Lymington, Hampshire. (95 Beds.) RESIDENT SENIOR HOUSE OFFICER (medical) required 1st February, 1958.

Applications, with copies of testimonials, should be forwarded as soon as possible to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

MAIDSTONE. KENT COUNTY OPHTHALMIC AND AURAL HOSPITAL. (113 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE SURGEON in the Ophthalmic Department of the above Hospital. The Hospital is recognised by the Examining Board for the F.R.C.S. and the D.O. Salary £819 10s. a year less £150 a year for residential emoluments.

Applications should be forwarded to the Administrative Officer, Kent County Ophthalmic and Aural Hospital, Church-street, Maidstone.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the pre-registration post of HOUSE SURGEON. 6 months' appointment. Post vacant mid-January, 1958. Salary at the rate of £467 10s.–£577 10s. A deduction at the rate of £125 a year is made for board and lodging, and other services provided.

Applications should be forwarded, as soon as possible, to the Administrative Officer at the Hospital.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. Salary £819 10s. p.a. less £150 p.a. for board and lodging. Post vacant February, 1958.

Applications to the Administrative Officer at the Hospital.

MANCHESTER. SPRINGFIELD HOSPITAL, Crumpsall, MANCHESTER, 8. SPRINGFIELD AND SWINTON HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER at this Mental Hospital of over 750 Beds. Period of tenure, 4 years in the first instance. Modern methods of investigation and treatment are carried out. Facilities will be granted for attendance at the course for D.P.M. of the University of Manchester (with the Department of Psychiatry of which this Hospital is associated). Preference given to candidates who have previous general hospital and/or psychiatric experience. Accommodation is available for a single person. Terms and conditions of the National Health Service apply. Further particulars can be obtained from, and the Hospital may be visited by arrangement with, the Medical Superintendent.

Applications, giving details of age, experience, &c., and the names of 3 referees, to the Medical Superintendent as soon as possible.

MANCHESTER REGIONAL HOSPITAL BOARD. Salford HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for post of REGISTRAR in Surgery (Resident Surgical Officer) at Salford Royal Hospital. Previous experience in surgery essential, F.R.C.S. or higher surgical qualifications desirable.

Applications, together with names of 2 referees, to be sent to Group Secretary, Salford Royal Hospital, Salford, 3, before 4th January, 1958.

MANCHESTER REGIONAL HOSPITAL BOARD. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of REGISTRAR in Radiotherapy at the Christie Hospital and Holt Radium Institute, Manchester. Candidates must hold either the Diploma in Radiotherapy or an F.R.C.S. or M.R.C.P.

Applications, with full details, to be forwarded to the Group Secretary, Withington Hospital, Manchester, immediately.

MANCHESTER, 20. GROUP PATHOLOGY LABORA-TORY, WITHINGTON HOSPITAL. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT PATHOLOGIST (Senior House Officer grade). Vacant now. Tenable for 12 months. Previous experience in pathology not essential, the post affording opportunities for gaining experience in all branches of clinical pathology. Laboratory recognised for the Dip. Path.

Applications, stating age, qualifications, present post, experience and the names of 2 referees, to be forwarded to the Group Secretary immediately.

MANCHESTER, 20. WITHINGTON HOSPITAL. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (surgical) including casualty duties. Vacant immediately. The post is recognised by the Royal College of Surgeons for the final F.R.C.S. examination, and possession of the primary F.R.C.S. will be an advantage. The Hospital is recognised by the University of Manchester for the teaching of undergraduate students.

Applications, with full details, to the Group Secretary immediately.

MANCHESTER, 23. WYTHENSHAWE HOSPITAL. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in Plastic Surgery. Vacant 1st February, 1958. This is the only House Officer post for a Plastic Surgery Unit of 71 Beds where the candidate appointed will spend most of his time, but in addition there are some general surgical duties.

Applications, with the names of 2 referees, to the Group Secretary, Withington Hospital, Manchester, 20.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the following posts :—

RESIDENT SURGICAL OFFICER (Registrar grade).
SENIOR HOUSE OFFICER.
HOUSE OFFICER (pre-registration surgical post).

Application forms may be obtained from the undersigned.

H. R. NORTH, General Superintendent.
Manchester Royal Eye Hospital.

MANCHESTER. UNITED MANCHESTER HOSPITALS. SAINT MARY'S HOSPITALS, MANCHESTER. Applications are invited for the post of SENIOR HOUSE OFFICER in Obstetrics, vacant shortly. Applicants must have had previous hospital experience in general medicine and surgery, and in obstetrics. The post is recognised for the purposes of the M.R.C.O.G. examination. The duties involve clinical responsibility for mothers and babies, and supervision of the work of pre-registration house officers is also included. The appointment is for 12 months. National scale.

Application forms may be obtained from the undersigned, and returned not later than 3rd January, 1958.

A. R. WISE, General Superintendent.
Saint Mary's Hospitals, Whitworth Park, Manchester, 13.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. 2 SENIOR HOUSE OFFICERS (surgical) to commence on 1st April and 8th May, 1958. Whole-time, mainly non-resident training posts, tenable for 6 months, renewable for a second 6 months. Duties allotted in Orthopædic, Surgical Outpatients and General Surgical Units in rotation. Resident alternate nights for about 3 months when attached to Orthopædic Unit.

Application form obtainable from the Secretary, to be returned by 18th January, 1958.

MONTROSE, ANGUS, SCOTLAND. ROYAL MENTAL HOSPITAL. (944 Beds.) Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (Male or Female). An attractive, self-contained, furnished house is available for a married man. Single furnished quarters are also available. All subject to appropriate deductions. Previous experience in psychiatry is not essential. Salary and conditions of service in accordance with national scale.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, should be forwarded immediately to the Physician-Superintendent.

NORTHAMPTON GENERAL HOSPITAL. (500 Beds.) Vacancy 1st February, 1958, for SENIOR HOUSE OFFICER, E.N.T. Department. Recognised for F.R.C.S. and for D.L.O. Appointment to 30th September, 1958, in first instance.

Applications as soon as possible to S. G. HILL, Superintendent.

NORTHAMPTON (near). CREATON HOSPITAL. (138 Beds.) Applications are invited from suitably qualified medical practitioners for the post of SENIOR HOUSE OFFICER. The Hospital has 138 Beds, and is for the treatment of both pulmonary and non-pulmonary tuberculosis. There is a major thoracic surgical unit for tuberculosis and non-tuberculous diseases of the chest.

Applications, stating age, experience and qualifications, together with the names and addresses of 2 referees, should be sent to the Secretary, Northampton and District Hospital Management Committee, General Hospital, Northampton, within 7 days of the appearance of this advertisement.

NOTTINGHAM CITY HOSPITAL. (811 Beds.) Applications are invited for the post of RESIDENT PATHOLOGIST (Senior House Officer). Previous experience an advantage. Post vacant 16th January, 1958.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM EYE HOSPITAL. 2 Senior House OFFICERS required, duties to commence about the middle of January. Salary and conditions of service in accordance with Ministry regulations. There is a flat available for 1 of the successful candidates.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary, General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. 2 Senior House OFFICERS (orthopædic and fracture) required (January and February, 1958). Post offers exceptional experience in traumatic surgery.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Senior House OFFICER (surgical) required on 25th January, 1958.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary, General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Resident pre-registration HOUSE SURGEONS required, 4th February, 5th February.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Senior House OFFICER (anæsthetics) required about 14th January, 1958. The post is recognised for the D.A. and the F.F.A. R.C.S. This is a busy general hospital, giving experience in all branches of surgery.

Applications, stating age, nationality, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary.

ORPINGTON HOSPITAL, Orpington, Kent. House SURGEON required. Pre-registration post, now vacant. Good experience in large, mainly acute, hospital.

Apply Surgeon-Superintendent, with copies of 2 recent testimonials.

PLYMOUTH. MOUNT GOLD ORTHOPÆDIC HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER for the Orthopædic and Fracture Service, centring on Mount Gold Orthopædic and associated hospitals. Post recognised by R.C.S.

Applications, stating age, qualifications with dates, &c., and with copies of 2 recent testimonials, to be forwarded to the Secretary, Mount Gold Hospital, Plymouth, within 14 days of this advertisement appearing.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL. Vacancies exist in the following department:—

SENIOR HOUSE OFFICER in Surgery, vacant 17th February, 1958. Recognised for the F.R.C.S.

HOUSE SURGEONS (pre-registration posts), vacancies now, 1st and 4th January, 1958. Recognised for the F.R.C.S. Greenbank Road Hospital.

In all cases send names of 3 referees to the Group Secretary, 7, Nelson-gardens, Stoke, Plymouth.

PONTYPRIDD (near). EAST GLAMORGAN HOSPITAL. CHURCH VILLAGE. (316 Beds and large Outpatient Department, Committee's Base Hospital serving population of 174,000. Recognised for D.Obst.R.C.O.G., F.R.C.S., D.C.H., F.F.A. R.C.S., D.A.)

SENIOR HOUSE OFFICER (obstetrics and gynæcology), to commence 13th February, 1958.

SENIOR HOUSE OFFICER (surgery), to commence 1st March. 1958.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent immediately to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

POOLE GENERAL HOSPITAL, Poole, Dorset. (310 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. RESIDENT OBSTETRIC OFFICER (Senior House Officer) required 20th January, 1958. Post recognised for D.Obst.R.C.O.G.

Applications to the Hospital Secretary.

PRESTON (near), LANCASHIRE. WHITTINGHAM HOSPITAL. SENIOR HOUSE OFFICER. Applications are invited for this post in the largest mental hospital in the country, where all modern treatment is undertaken, including electro-encephalography for the area. Facilities will be given for study either for the D.P.M. in Manchester University or for the M.R.C.P. at a large general hospital a few miles away. This Hospital is well situated in a country district with easy access to Preston, Blackpool, and Southport. If single, there are comfortable quarters available.

Applications, endorsed "Medical Officer," giving details of experience and names and addresses of 3 referees, to be addressed to the Medical Superintendent, Whittingham Hospital, near Preston, and be received as soon as possible.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEONS required for General Surgical Unit, term commencing 1st February, 1958.

Applications to Group Medical Superintendent.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEON required for Orthopædic Unit, term commencing 1st February, 1958.

Applications to Group Medical Superintendent.

PAISLEY AND DISTRICT MATERNITY UNIT. House OFFICERS required for above Unit, term commencing 1st February, 1958.

Applications to Group Medical Superintendent, Royal Alexandra Infirmary, Paisley.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

(1) Saint Mary's Hospital

(*a*) Applications are invited for the appointment of SENIOR HOUSE OFFICER (medical), vacant now. Duties will be mainly in the acute medical wards and outpatients, but there will be some duties in the Geriatric Assessment Unit of 76 Beds. The appointment affords an opportunity of seeing large numbers of acute cases and is an excellent one for those studying for a higher medical qualification.

(*b*) Pædiatric (Pædiatric Unit of 53 Beds).

HOUSE PHYSICIAN. The post is recognised for candidates preparing for the D.C.H. Vacant 1st February, 1958.

(*c*) Surgery (130 surgical beds).

HOUSE OFFICERS (pre-registration). Vacant 30th January, 1958, 1st February, 1958, 9th February, 1958, 11th February, 1958.

(*d*) Medical (74 medical beds).

HOUSE OFFICERS (pre-registration). Vacant 31st January, 1958, 12th February, 1958.

(2) Royal Portsmouth Hospital

(*a*) Pædiatric and Medical (total of 30 Beds).

HOUSE OFFICER (pre-registration). Vacant 1st February, 1958.

(*b*) Orthopædic Department (104 Beds).

(i) SENIOR HOUSE OFFICER required. Vacant now.

(ii) HOUSE OFFICER (pre-registration). Vacant now.

(*c*) Medical (61 medical beds).

HOUSE OFFICERS (pre-registration). Vacant 19th January, 1958, 10th February, 1958.

(3) Queen Alexandra Hospital

(*a*) SENIOR HOUSE OFFICER (78 medical beds and 24 dermatology beds). General medicine and dermatology. Vacant 29th January, 1958.

(*b*) SENIOR HOUSE SURGEON (87 surgical beds). Vacant 1st January, 1958.

(*c*) HOUSE OFFICER. Vacant 12th February, 1958.

(*d*) HOUSE OFFICER (pre-registration). Vacant 1st February, 1958.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER for E.N.T. Department, Royal Berkshire Hospital, Reading (40 Beds). Post recognised for D.L.O.

Applications, stating age, nationality, experience and qualifications, together with names of 2 referees, should be sent to Group Secretary, 3, Craven-road, Reading.

ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIANS (pre- or post-registration) required for Birch Hill Hospital. Post offers wide experience in general medicine. Staff of 5 residents in the Medical Department.

Apply at once to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale.

ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade) in the Department of Pathology of the Rochdale Group of hospitals. A new Department of Pathology is now being completed and will be opened early next year. The duties will consist mainly of clinical pathology, also general and emergency work and supervision of the blood banks. Previous pathology experience is not essential. Post vacant end of year.

Applications, giving usual particulars and names and addresses of 2 referees, to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancashire, at once.

ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (resident) required early January, 1958. Pre- or post-registration doctors eligible for this post which is recognised for 6 months' F.R.C.S. experience.

Apply at once to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale.

ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. BIRCH HILL HOSPITAL. SENIOR HOUSE OFFICER (obstetrics and gynæcology) required 1st January, 1958. The post is for 12 months in the first instance and is recognised for the D.Obst.R.C.O.G.

Apply at once to the Group Secretary, Central Offices, Birch Hill Hospital, Rochdale.

ROCHFORD, ESSEX. GENERAL HOSPITAL. (620 Beds.) Required, Locum REGISTRAR for Chest Unit at the General Hospital, Rochford, on a month-to-month basis, pending post being filled by the Regional Hospital Board. Post vacant 1st January, 1958.

Apply immediately to the undersigned.

J. C. FIELD, Secretary,
Management Committee Offices,
General Hospital, Rochford, Essex.

RYDE. ROYAL I.W. COUNTY HOSPITAL. Isle of WIGHT GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. CASUALTY AND ORTHOPÆDIC OFFICER required end January, 1958, at the above Hospital, either as Registrar (£935–£1061 10s.) or as Junior Hospital Medical Officer (£852 10s.–£55–£1182 10s.). The appointment is resident, married or single accommodation being available, and is recognised for the F.R.C.S.

Forms of application may be obtained from the Group Secretary, Hospital Management Committee, Clatterford House, Carisbrooke, I.W., and should be returned not later than 10th January, 1958.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. Pædiatrics. Dundee General Hospitals. Applications are invited for the post of SENIOR REGISTRAR in Pædiatrics at Dundee Royal Infirmary (534 Beds) and Maryfield Hospital, Dundee (370 Beds), the main teaching hospitals associated with the University of St. Andrews. The duties will include teaching of undergraduates. Salary and conditions of service in accordance with national agreement.

Further particulars and forms of application from the Secretary to the Board, "Braeknowe", 430, Blackness-road, Dundee, with whom applications must be lodged not later than 4th January, 1958.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. REGISTRAR to the Respiratory Diseases Unit, from 7th March, 1958, for the period of 1 year in the first instance. Duties will be with either the Edinburgh Royal Victoria and Associated Hospitals or the Edinburgh Northern Group of Hospitals and may involve work with both tuberculosis and non-tuberculous diseases of the chest. The post is associated with the Department of Tuberculosis and Diseases of the Respiratory System, University of Edinburgh, and the holder will be expected to assist with teaching and research.

Apply, giving particulars of age, qualifications and previous experience, and the names of 2 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 11th January, 1958.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance:—

SENIOR REGISTRAR in Pathology based at the Southern General Hospital, Glasgow.

SENIOR REGISTRAR in Radiotherapy based at the Western Infirmary, Glasgow.

2 REGISTRARS in Surgery based at the Western Infirmary, Glasgow, with duties for a period at the Lewis Hospital, Stornoway.

REGISTRAR in Obstetrics and Gynæcology based at Cresswell Maternity Hospital, Dumfries.

REGISTRAR in Anæsthetics based at the Victoria Infirmary, Glasgow, with duties also at Hairmyres Hospital, East Kilbride.

REGISTRAR in Medicine based at the Medical Unit, Gartloch Hospital, Gartcosh, Glasgow.

REGISTRAR in Ophthalmology based at the Glasgow Eye Infirmary.

REGISTRAR in Psychiatry based at the Southern General Hospital, Glasgow. This appointment is in association with the University Department of Psychological Medicine, where there is a formal postgraduate training course in psychiatry.

REGISTRAR in Medicine based at the Southern General Hospital, Glasgow.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64 West Regent-street, Glasgow, C.2, by 11th January, 1958.

SCUNTHORPE. WAR MEMORIAL HOSPITAL. House PHYSICIAN (1 of 2). Applications invited for pre-registration/Senior House Officer post, vacant late January. Modern Hospital with busy department including medicine, pædiatrics, skins, and eyes, with busy outpatient clinics offering good experience.

Applications, naming 2 referees, to Group Secretary, Scunthorpe Hospital Management Committee.

SHOREHAM-BY-SEA, SUSSEX. SOUTHLANDS HOSPITAL. (120 acute surgical, 50 orthopædic beds.) 2 HOUSE SURGEONS required for general surgical duties, pre- or post-registration. Both posts recognised by R.C.S. for Fellowship.

Applications to Secretary, Southlands Hospital, Shoreham-by-Sea.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.

SHOREHAM-BY-SEA, SUSSEX. SOUTHLANDS HOSPITAL. Locum Tenens HOUSE SURGEON, general surgical duties, immediately.

Applications to Secretary, Southlands Hospital, Shoreham-by-Sea.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.

SHOREHAM-BY-SEA, SUSSEX. SOUTHLANDS HOSPITAL. (411 Beds.) Applications are invited for the post of OBSTETRIC AND GYNÆCOLOGICAL REGISTRAR (55 and 30 Beds). M.R.C.O.G. preferred. Post vacant 1st April, 1958.

Forms of applications may be obtained from the undersigned.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.
129, Brighton-road, Worthing, Sussex.

SHREWSBURY. EYE, EAR AND THROAT HOSPITAL. SENIOR HOUSE OFFICER (ophthalmic). Eye Unit, 35 Beds. Post recognised for the D.O.M.S. Vacant 9th February, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL. (500 Beds.) HOUSE PHYSICIAN—pre-registration candidates eligible. Vacant 31st January, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY. CHILDREN'S UNIT. SENIOR HOUSE OFFICER or HOUSE OFFICER (pædiatric). Recognised for D.C.H. 6-month appointment. The Unit consists of medical, surgical and fever beds. Vacant mid-January, 1958. Married quarters available.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

STOKE-ON-TRENT GROUP. Medical Registrar (chest diseases). Duties alternating between Cheshire Joint Sanatorium, City General Hospital, and Stoke-on-Trent Chest Clinic. Post offers wide experience in the investigation and medical and surgical treatment of tuberculosis and other chest diseases. Resident or non-resident. Possibility of married accommodation becoming available later.

Application forms from Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent, to be returned by 6th January, 1958.

SHEFFIELD, 5. CITY GENERAL HOSPITAL. DEPARTMENT OF PATHOLOGY, GROUP LABORATORY. Applications are invited for the appointment of SENIOR HOUSE OFFICER (clinical pathology). Resident accommodation is available and optional. Opportunities for training in morbid anatomy, biochemistry, haematology and bacteriology. The work of this and the associated hospitals offers excellent experience to graduates who wish to make pathology their permanent career. The post is recognised for the D.Path.

Apply, giving details of age, qualifications, present and previous appointments with dates, and the names of 2 persons to whom reference may be made, to the Group Secretary, Nether Edge Hospital, Sheffield, 11.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. ROYAL INFIRMARY. Applications invited for the non-resident post of REGISTRAR in the Rupert Hallam Department of Dermatology at the above Hospital.

Applications, stating age, qualifications and experience, with the names of 3 referees, should be sent to the Chief Administrative Officer, United Sheffield Hospitals, West-street, Sheffield, 1, not later than 4th January, 1958.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. ROYAL INFIRMARY. Applications invited for 2 posts of SENIOR HOUSE OFFICER in the Department of Neurological Surgery. Both posts vacant 15th January, 1958. Previous experience in medical or surgical neurology welcome but not essential. One of these posts would be suitable for intending physicians as it offers wide experience in neurological methods and diagnosis. Both these posts, if required, may be held for 6 months only.

Applications, with full details and the names of 3 referees, should be sent to the Superintendent, Royal Infirmary, Infirmary-road, Sheffield, 6.

SOUTHAMPTON GENERAL HOSPITAL. (474 Beds.) RESIDENT HOUSE SURGEON required. Pre-registration candidates eligible.

Applications, with copies of recent testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (anæsthetics) for the Anæsthetic Department of the Southampton Group of hospitals. Special facilities for working for F.F.A. R.C.S. and D.A.

Applications, with copies of testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds.) RESIDENT HOUSE SURGEON required. Pre-registration candidates eligible.

Applications, with copies of recent testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTH BRENT, DEVON. DIDWORTHY CHEST HOSPITAL. Applications are invited from registered medical practitioners for the post of ASSISTANT MEDICAL OFFICER (Junior Hospital Medical Officer grade) at the above Hospital. This is a Hospital of 128 Beds for the treatment of pulmonary tuberculosis and includes a major thoracic surgery unit. Unfurnished bungalow available on Hospital estate.

Applications, stating age, nationality and qualifications, together with names of 2 referees, should be sent, as soon as possible, to the Group Secretary, Plymouth Special Hospital Management Committee, 8, Nelson-gardens, Stoke, Plymouth.

STOCKPORT INFIRMARY. Applications are invited for the post of SENIOR HOUSE OFFICER (Resident Surgical Officer), vacant early February, 1958. The post is recognised for the F.R.C.S.

Applications, stating age, experience and qualifications, together with copies of 2 testimonials, to be addressed to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

STRATFORD-ON-AVON HOSPITAL. (163 Beds.) RESIDENT HOUSE SURGEON. New post providing excellent experience.

Applications from fully registered or pre-registration applicants, with 2 recent testimonials, to Hospital Secretary.

SUNDERLAND. ROYAL INFIRMARY, Durham-road, SUNDERLAND. (300 Beds.) HOUSE OFFICER or SENIOR HOUSE OFFICER (Male) according to experience, required for duties in gynæcology and urological units. Post vacant now. Provisionally registered practitioners may apply.

Apply to Hospital Secretary, giving the names and addresses of 2 referees.

SURBITON GENERAL HOSPITAL, Ewell-road, Surbiton, SURREY. RESIDENT JUNIOR HOUSE OFFICER (surgical) required. Pre-registration post. Duties include casualty work under direction of Resident Surgical Officer.

Applications, stating age, qualifications, nationality, and enclosing copies of 2 testimonials, to the Administrative Officer.

SWANSEA HOSPITAL, Swansea. (413 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of CASUALTY OFFICER of Junior Hospital Medical Officer grade, at the above Hospital. Resident or non-resident. Immediate vacancy.

Full particulars, stating age, qualifications and experience, together with the names of 2 referees, should be forwarded to the Secretary of the Hospital. T. E. JONES, Group Secretary.

SWANSEA HOSPITAL, Swansea. (413 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON at the above Hospital. The post is recognised for pre-registration purposes. The Hospital is a busy acute general hospital and offers excellent experience. Vacancy 1st February, 1958.

Applications, with full particulars and copies of 2 recent testimonials, should be sent to the Secretary of the Hospital.

T. E. JONES, Group Secretary.

TORQUAY. TORBAY HOSPITAL. (166 general beds.) RESIDENT HOUSE OFFICER (surgical), Male or Female, required approximately 15th December, 1957. Post recognised for F.R.C.S. and pre-registration purposes. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, nationality and age, together with copy testimonials (quoting reference F.955/84), to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

TORQUAY. TORBAY HOSPITAL. Resident Casualty OFFICER (Senior House Officer status) required approximately 23rd December, 1957. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, nationality, age (quoting ref. F.955/86), with copy testimonials, to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

WALLASEY. VICTORIA GENERAL HOSPITAL. Applications are invited for the appointment of SENIOR HOUSE OFFICER in Pathology. The department is in the charge of a full-time Consultant Pathologist and is made up of separate Laboratories. Salary and conditions of service in accordance with Whitley Council agreements.

Applications, with names and addresses of 3 referees, to Group Secretary, North Wirral Hospital Management Committee, Victoria General Hospital, Wallasey.

WARRINGTON INFIRMARY. (172 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST (Male or Female), graded as Senior House Officer. The Hospital is recognised for the D.A. examination. Salary is £819 10s. p.a. less a deduction of £150 p.a. for residential emoluments.

Applications, stating qualifications and experience, should be sent to— HENRY L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee.
c/o General Hospital, Warrington, Lancs.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) ORTHOPÆDIC HOUSE SURGEON (with certain casualty duties) required. Post recognised for F.R.C.S.(Eng.) examination. Intermediate or senior post, depending on experience, for orthopædic unit (30 Beds). The orthopædic service is in the charge of a Consultant and Registrar closely associated with a postgraduate teaching hospital.

Applications with copies of 2 testimonials to the Administrator.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) Applications are invited for the post of HOUSE SURGEON at the above Hospital. This is a pre-registration post and is recognised for F.R.C.S. Salary according to the National Health Service scale.

Applications, with copies of recent testimonials, to the Administrator.

WELSH REGIONAL HOSPITAL BOARD. Registrar in Anæsthetics, based Bridgend General Hospital. Hospital recognised for F.F.A.R.C.S. Resident/non-resident. Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WESTON-SUPER-MARE GENERAL HOSPITAL. (107 Beds.) Applications are invited from registered medical practitioners for the pre-registration appointment (resident) of HOUSE PHYSICIAN, vacant 1st February, 1958.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WESTON-SUPER-MARE GENERAL HOSPITAL. (107 Beds.) Applications are invited from registered medical practitioners for the pre-registration appointment (resident) of HOUSE SURGEON, vacant 1st February, 1958.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WIGAN AND LEIGH HOSPITAL MANAGEMENT COMMITTEE. ROYAL ALBERT EDWARD INFIRMARY, WIGAN. HOUSE SURGEON, pre-registration post, vacant early January.

Applications, with names of 2 referees, to Secretary, Knowsley House, Wigan.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOS-PITAL. (315 Beds.) HOUSE SURGEON to the Senior Surgeon. Post vacant 16th February.

Applications, with copies of 2 testimonials, to the Group Secretary.

WOKING. THE ROWLEY BRISTOW ORTHOPÆDIC HOSPITAL, PYRFORD, WOKING, SURREY. (200 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON (Senior House Officer grade), vacant mid-February. The post is recognised for the F.R.C.S. examination and will include 1 session per week at St. Thomas's Hospital, London.

Applications should reach the Secretary within 14 days of the date of this advertisement.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) HOUSE OFFICER (pre-registration) E.N.T. Department, recognised for the D.L.O. and F.R.C.S. examinations. Vacant 1st March.

Apply, giving age and qualifications, with copies of 2 testimonials, to the Hospital Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) Vacancies for Pre-registration HOUSE OFFICERS (medicine) occur on 2nd, 17th and 22nd January.

Please apply, with copies of 2 testimonials, to Hospital Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) Pre-registration HOUSE OFFICER (pædiatrics) required. Post recognised for D.C.H. Vacant 20th January, 1958.

Apply, giving age and qualifications, with copies of 2 testimonials, to the Hospital Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) Pre-registration HOUSE OFFICERS. Vacancies in surgery occur on 1st, 6th, 11th and 23rd January, 1958.

Apply, giving age and qualifications, with copies of 2 testimonials, to the Hospital Secretary.

WORCESTER ROYAL INFIRMARY. House Surgeon (pre-registration or otherwise) required mid-January for general surgery post at this busy general hospital of 213 Beds. The appointment offers wide and varied experience and is recognised for the F.R.C.S. examinations.

Applications to Hospital Secretary.

WORCESTER ROYAL INFIRMARY. House Surgeon (pre-registration or otherwise) required mid-January for Orthopædic Department of this busy general hospital of 213 Beds. The appointment offers wide and varied experience.

Applications to Hospital Secretary.

WORCESTER ROYAL INFIRMARY. (213 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER in Medicine (Resident Medical Officer), vacant early January. The post is of 1 year's duration and although dealing mainly with acute medicine the post also covers some work in infectious diseases and geriatrics.

Applications, with copies of 3 recent testimonials, to be sent to the Secretary.

WREXHAM. MAELOR GENERAL HOSPITAL. (591 Beds.) Applications are invited for the posts of HOUSE SURGEON (2) at the above Hospital, to commence duties on 1st February, 1958. The appointments are recognised for the diploma of F.R.C.S. (England, Edinburgh, and Ireland) and are pre-registration posts.

Applications, stating age, nationality, qualifications and experience, with copies of 2 recent testimonials, to be sent to the Group Secretary, Maelor General Hospital, Wrexham, as soon as possible.

WREXHAM (near). TREVALYN MANOR MATERNITY HOSPITAL, ROSSETT, near WREXHAM. (47 Beds.) Applications are invited for the post of HOUSE SURGEON at the above Hospital, to commence duties on 1st February, 1958. The hospital is a Part II midwifery training school and deals with normal and abnormal midwifery.

Applications, stating age, nationality, qualifications and experience, with copies of 2 recent testimonials, to be sent to the Group Secretary, Maelor General Hospital, Wrexham, as soon as possible.

WREXHAM. WAR MEMORIAL HOSPITAL. (230 Beds.) Applications are invited for the posts of HOUSE SURGEON (2) at the above Hospital, to commence duties on the 1st February, 1958. The appointments are recognised for the Diploma of F.R.C.S. (England and Edinburgh) and are pre-registration posts.

Applications, stating age, nationality, qualifications and experience, with copies of 2 recent testimonials, to be sent to the Group Secretary, Maelor General Hospital, Wrexham, as soon as possible.

OTTAWA CIVIC HOSPITAL, Ottawa, Canada (General— 800 Beds), invites applications to fill an appointment as RESIDENT in Medical Department from 1st July, 1958, to 30th June, 1959. This is a senior appointment for a man who proposes to write Fellowship examinations in Canada in the field of internal medicine and the appointment involves teaching graduate interns. Salary $200 per month, plus room and board.

Applications, stating age, qualifications, experience, and names of 2 referees, should be forwarded to Superintendent, Ottawa Civic Hospital, Ottawa, Canada.

MICHIGAN, U.S.A. OAKWOOD HOSPITAL, Dearborn, MICHIGAN. Applications are invited for 1 or 2-year approved GENERAL PRACTICE RESIDENCY in modern 234-Bed General Hospital 10 miles from Detroit. Excellent facilities. Hospital approved for exchange-visitor programme. Beginning monthly salary $250 if single, $300 if married. Free housing.

Apply: Director.

ST. JOHN'S, NEWFOUNDLAND, CANADA. GENERAL HOSPITAL. (475 Beds.) Applications are invited for the post of JUNIOR ASSISTANT PATHOLOGIST. Salary $4500 p.a. At least 2 years' postgraduate training in surgical and autopsy pathology desirable. This post is recognised by the Royal College of Physicians and Surgeons in Canada. Transportation to St. John's will be arranged and paid by the Hospital.

Applications, stating age, qualifications and experience, together with the names of 2 referees, should be sent immediately to Dr. E. WILSON, Superintendent, General Hospital, St. John's, Newfoundland, Canada.

ST. JOHN'S, NEWFOUNDLAND, CANADA. GENERAL HOSPITAL. (475 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST. Salary $3600 p.a., less $660 for board, maintenance, &c. Previous experience in anæsthetics desirable. The post offers experience for all types of anæsthesia and is recognised by the Royal College of Physicians and Surgeons in Canada. Transportation to St. John's will be arranged and paid by the Hospital.

Applications, stating age, qualifications and experience, together with the names of 2 referees, should be sent immediately to Dr. E. WILSON, Superintendent, General Hospital, St. John's, Newfoundland, Canada.

Public Appointments

LONDON COUNTY COUNCIL. Applications are invited from medical practitioners practising in Camberwell area under National Health Service for appointment as VISITING MEDICAL OFFICER to Picton Lodge Home for 73 old and infirm people in Picton-street, S.E.5. Remuneration £40 a year plus fees receivable from Executive Council in respect of residents and resident staff who may be on National Health Service list.

Particulars and application forms from Medical Officer of Health (PH/D.1/2277), County Hall, Westminster Bridge, S.E.1, and returnable by 10th January, 1958.

LONDON COUNTY COUNCIL. Applications invited from registered medical practitioners for appointment as Whole-time MEDICAL OFFICER in Public Health Department. Inclusive salary scale £1050–£1475. Commencing salary dependent on Local Government service. No emoluments. Duties primarily connected with child health. Experience in maternity and child welfare work and the school health service and possession of Diploma in Public Health advantageous.

Application forms from Medical Officer of Health (PH/D. 1/2316), The County Hall, Westminster Bridge, S.E.1, returnable by 10th January.

AMENDED ADVERTISEMENT

BARNSLEY. COUNTY BOROUGH OF BARNSLEY. PUBLIC HEALTH DEPARTMENT. Applications are invited from registered medical practitioners who hold the Diploma in Public Health for the appointment of DEPUTY MEDICAL OFFICER OF HEALTH and DEPUTY SCHOOLS MEDICAL OFFICER. The salary will be on the scale £1340–£55(4)–£50–£1610, commencing at £1560 p.a. and rising by 1 increment of £50 to £1610 p.a. Candidates should have had experience in all branches of the public health and school health services, and will be required to devote the whole of the time to the duties of these offices. The possession of a car is desirable, in which event consideration will be given to the payment of a car allowance. The appointment will be subject to the conditions of service laid down by the Medical Whitley Council Committee C, and to any other general conditions of employment in operation within the corporation from time to time. The post is superannuable, and the candidate selected will be required to pass a medical examination before appointment, and the appointment will be subject to 3 months' notice on either side.

Applications, stating age, full particulars and details of experience and qualifications, together with the names and addresses of 3 referees, should be sent to the Medical Officer of Health, Public Health Department, Town Hall, Barnsley, to arrive not later than 11th January, 1958. Canvassing will disqualify. A. E. GILFILLAN, Town Clerk.

Town Hall, Barnsley. 13th December, 1957.

BUCKS COUNTY COUNCIL. Applications are invited from registered medical practitioners for the appointment of ASSISTANT COUNTY MEDICAL OFFICER in the Aylesbury area. Preference will be given to applicants possessing a Diploma in Public Health or a Diploma in Child Health, and experience in maternity, school medical and child welfare work. Salary within the scale £1050–£1475 p.a., the commencing salary being fixed according to qualifications and experience. Travelling and subsistence allowances on the County Council's scale will be paid. The appointment is superannuable and subject to medical examination.

Further particulars and forms of application may be obtained from the County Medical Officer, County Offices, Aylesbury, to whom completed applications must be returned by 20th January, 1958. R. E. MILLARD, Clerk of the Bucks County Council.

County Hall, Aylesbury, December, 1957.

DERBYSHIRE COUNTY COUNCIL. County Health DEPARTMENT. MATERNAL AND CHILD WELFARE MEDICAL OFFICER (Female). Applications are invited from fully qualified medical practitioners for this whole-time superannuable post. Candidates should be experienced in antenatal work, midwifery, and children's diseases, as they will be required to hold consultations at the Council's maternity and child welfare clinics and centres, and to perform such other duties as may be required. Salary £1050–£50–£1200–£55–£1475 p.a., plus a car allowance.

Particulars and application forms are obtainable from Dr. J. B. S. MORGAN, County Medical Officer, St. Mary's-gate, Derby, and should be returned to him duly completed not later than 6th January, 1958.

EXETER. CITY AND COUNTY OF THE CITY OF EXETER. SCHOOL MEDICAL OFFICER AND ASSISTANT MEDICAL OFFICER OF HEALTH. The duties will be mainly in connection with the school health and child welfare services, but the appointed candidate will assist in other sections of the department. The successful candidate will gain administrative experience in school health work. The possession of a D.P.H. or D.C.H. would be an advantage. Whitley scales and conditions. Salary £1050–£50–£1200–£55–£1475. Commencing salary according to experience. Casual car user allowance.

Application forms from Dr. E. D. Irvine, Medical Officer of Health and Principal School Medical Officer, 5, Southernhay West, Exeter, to whom they should be returned not later than 31st January, 1958. C. J. NEWMAN, Town Clerk.

BECHUANALAND PROTECTORATE. Medical Officers with qualifications registrable in United Kingdom required for general duties. "R" practitioners, i.e., practitioners liable for call-up under the National Service Acts, may apply, and if appointed, will be granted indefinite deferment of call-up on completion of a minimum period of 2 years. Appointment can be either on 2 years' probation to pensionable establishment or on 30 months' contract with gratuity (taxable) of 12½% of aggregate emoluments. Salary scale £940–£1515 p.a., starting salary determined by age and experience. Following non-pensionable allowances are payable:—

(*a*) Cost-of-living allowance 15½% of salary up to maximum of £170 10s. p.a. for married officers and half this rate for single officers.

(*b*) Special allowance of £60 p.a. for married officers and £30 for single officers.

(*c*) Education allowance (up to 3 children under age of 18 attending school outside the territory) of £120 p.a. for first child, £96 for second, and £72 for third.

Private practice permitted varying from station to station.

Quarters and heavy furniture provided at low rental. Free passages for officer, wife and up to 3 dependent children. Local leave permitted and generous home leave granted after each tour. Income-tax at low local rates.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD. 117/76/02).

GOVERNMENT OF WESTERN NIGERIA. Applications invited from Male doctors for following posts in the Medical Department of the Western Region of Nigeria:—

MEDICAL OFFICER for general medical work including emergency surgery in district hospitals and general health work including supervision of rural schools, maternity and child welfare clinics.

MEDICAL OFFICERS OF HEALTH who will normally be based at 1 of the larger urban centres in the Region, where they will be primarily responsible for public health administration of the area, with emphasis on sanitation and hygiene. Duties include school health, public health, education and propaganda, control of quarantinable diseases and possibly establishment and supervision of maternity, child welfare and tuberculosis centres. A candidate with special aptitude for teaching may be selected to take charge of new School of Hygiene for training of sanitary inspectors at Ibadan. Candidates should hold Diploma in Public Health.

PATHOLOGIST to organise and supervise a Regional Laboratory Service. Most hospitals in Region have small laboratories attached where routine work is performed, but the more complicated tests, sections, &c., will be the selected officer's concern at a Central Regional Laboratory. He will have to supervise and encourage the work of African Technicians which will necessitate travelling. Candidates must have experience in laboratory work.

Appointments (of 1 or 2 tours) may be:—

(*a*) from National Health Service, candidate retaining superannuation rights. Salary scale £1086–£1950 p.a., and gratuity (taxable) of 20% of aggregate salary on completion of appointment, or

(*b*) on short-term contract. Salary scale £1290–£2286 p.a., and gratuity (taxable) at rate of £37 10s. for each completed period of 3 months' service (including leave) payable on satisfactory completion of appointment.

Entry point in both cases determined by qualifications and experience. In addition, officers receive supplementary pay of £120 p.a.

Quarters provided at low rental. Taxes at local rates. Annual leave permissible: generous home leave after each tour of 18–24 months. Free return passages for officer, wife and children (up to 3).

Application forms from Director of Recruitment, Colonial Office, London, S.W.1, quoting (BCD. 117/410/018).

DUBLIN. LOCAL APPOINTMENTS COMMISSION. Position vacant. TEMPORARY COUNTY SURGEON, Kildare County Council. Salary scale £1517, with permission to engage in private practice plus the use of certain beds.

Application forms and further particulars from the Secretary, 45, Upper O'Connell-street, Dublin. Latest time for receiving completed application forms: 5.0 P.M. on 10th January, 1958.

Miscellaneous

Principal M.O. required for a large group of tea gardens in north east India early May, 1958, for 6 months. Operating surgical experience required. Would suit man reading for final F.R.C.S. Furnished bungalow, servants and transport provided. Free return passages for doctor and wife.—Apply with full details, qualifications and experience and recent testimonials to Address No. 355, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Korea. Doctor (Female) required with paediatric experience; age preferably between 26 and 40. Contract 1 year renewable. Salary £1000 p.a. Maintenance equipment allowances and fares paid. 1 month's holiday per year. Duties in Pusan, Korea.—Apply Foreign Relief Secretary, Save the Children Fund, 12, Upper Belgrave-street, S.W.1. Telephone SLOane 9171.

Applications are invited for the appointment of a Medical Officer with a leading British company in British West Africa. Applicants should not be more than 35 years of age and should have had good all-round experience since qualifying. Salary will be in accordance with age, experience and qualifications, but will not be less than £1600 p.a. In addition there are family allowances, free passages to and from West Africa and free furnished quarters. Membership of pension fund is compulsory. Tours of duty will be about 18 months, followed by leave on full pay.

Applications, giving full details of experience, should be made to the Principal Medical Officer, Unilever House, Blackfriars, London, E.C.4.

Doctor required in N.W. area willing to be "on call" on Saturdays. No surgery.—Address No. 358, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Histologic technicians, experienced. Excellent salary. —Write Congenital Heart Disease Research and Training Center, 629, South Wood-street, Chicago, Ill., U.S.A., giving full details.

"Alfona" is fat-free cow's milk to which has been added vegetable oils containing essential fatty acids suitable for atheroma cases.—Enquiries to ALFONAL, Shell-Mex House, Strand, London, W.C.2 (Telephone COV. 2211).

Doctors requiring applications, theses copied: Write to MANTON (WESTMINSTER) LTD., 98, Victoria-street, S.W.1 (VIC 0141), who are specialists.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Early surgical and medical instruments. Advertiser, engaged on historical study of early surgical instrument makers, would be glad to hear from anyone possessing 18th or early 19th century instruments, catalogues, &c.—Address No. 357, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Mr. Arthur Shaw (medical agent) anticipates the book which he has written will be published during 1958. Publication date will be announced later.

PUBLISHED by the PROPRIETORS, THE LANCET LIMITED, 7, Adam Street, Adelphi, in the County of London.
Printed by HAZELL, WATSON AND VINEY, LTD., Leigh Road, Slough and Aylesbury—Saturday, December 28, 1957.
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IT WAS RECENTLY reported (*Brit. med. J.*, 1: 444, 1957) that of 178 rheumatic patients, 25% could not take plain aspirin in adequate dosage.

Of this 25%, however, the great majority tolerated a modified aspirin such as Paynocil.

Not only are Paynocil tablets usually well tolerated by the stomach (even on the heavy dosage needed for rheumatoid arthritis), but they are extremely palatable, disintegrate instantly on the tongue without water, and cause no discomfort or unpleasant after-sensation.

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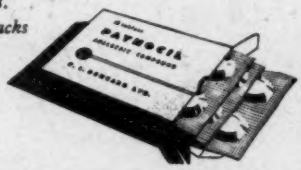

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Aminoacetic acid ..... 1½ grains

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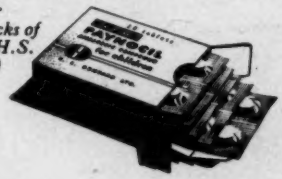

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